COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% AND HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA

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I hereby declare that the thesis entitled **"COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% AND HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA"** submitted towards partial fulfillment of the requirements for the award of **MD IN ANAESTHESIOLOGY** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Richa Jain,** Associate Professor, Department of Anaesthesiology, **Dr. Shikha Gupta,** Professor, Department of Anaesthesiology, DMCH. No part of this thesis has formed the basis for the award of any degree previously.

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LIST OF ABBREVIATIONS

SAB	Subarachnoid Block
LA	Local Anaesthetic
SA	Spinal Anaesthesia
SB	Sensory Block
MB	Motor Block
CNS	Central Nervous System
pKa	-log of acid dissociation constant
AMP	Adenosine Mono Phosphate
CVS	Cardiovascular System
MBS	Modified Bromage Score
MAP	Mean Arterial Pressure
I/V	Intravenous
ASA	American Society of Anaesthesiologists
TURP	Trans Urethral Resection of Prostate
BMI	Body Mass Index
PAC	Pre-anaesthetic Checkup
VAS	Visual Analogue Scale
OR	Operating Room
HR	Heart Rate
NIBP	Non Invasive Blood Pressure
SPO2	Oxygen saturation
HR	Heart Rate
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
ml/kg	milli-litre/ kilogram
mcg or µgm	microgram
cc	cubic centimeters
G	Guage
ml/sec	milli-litre/second
min	minute
PACU	Post Anaesthesia Care Unit
SD	Standard Deviation

ABSTRACT

Introduction: Subarachnoid Block is a preferred and popular mode of anesthesia in patients posted for lower limb surgeries due to its ease of administration and maintenance of spontaneous respiration. After the introduction of bupivacaine, it became the most commonly used intrathecal drug to produce adequate surgical anaesthesia. Reports started surfacing, concerning the incidences of CNS and CVS toxicity associated with this drug. Ropivacaine, another long acting local anaesthetic was introduced in the market. A few studies were done comparing the efficacy of various concentrations of ropivacaine but the efficacy and safety of 0.75% hyperbaric ropivacaine when compared to 0.5% hyperbaric bupivacaine was still not clear. With this background, the present study has been designed to evaluate the efficacy of 0.75% hyperbaric ropivacaine and 0.5% hyperbaric bupivacaine with fentanyl when administered in patients undergoing lower limb surgeries under spinal anaesthesia.

Objective: To compare the efficacy and safety, in terms of onset and duration of sensory and motor block, of hyperbaric 0.75% ropivacaine versus hyperbaric 0.5% bupivacaine in combination with fentanyl in spinal anaesthesia for lower limb surgeries.

Methods: A prospective randomized double blind controlled study was conducted on sixty patients of ASA grade I-III of either gender scheduled for lower limb surgeries under SA. Patients were allocated to one of the two groups according to computer generated random numbers. Both groups were given total 3 ml drug i.e. 2.5 ml of study drug with 25mcg fentanyl. The two study groups were recorded for duration of sensory block, onset of sensory and motor block, duration of motor block, need for first rescue analgesic and episodes of hypotension and bradycardia and compared in this study.

Results: Ropivacaine group (99.27 ± 11.79 min) took significantly longer time for two segment regression when compared with the bupivacaine group (85.17 ± 19.19 min) with P = 0.001. Both the groups showed comparable onset of sensory block, group R (6.30 ± 3.66 min) and group B (7.0 ± 5.37 min) with P= 0.812 and motor block, 9.4 ± 2.1 mins in group R and 8.2 ± 5.3 mins in group B with p = 0.25. The duration of motor block was significantly shorter in Group R (175.90 ± 40.81 mins) as compared to group B (205.07 ± 57.17 mins) with p = 0.052. When compared for the need for first rescue analgesic, bupivacaine group (300.73 ± 62.85 mins) had significantly longer duration of analgesia in comparison to ropivacaine group (264.33 ± 46.72 mins) with p= 0.013. In our study, 7 out of 30 patients (23.3%) in ropivacaine group and 16 patients (53.3%) in bupivacaine group had hypotension requiring ephedrine boluses, p = 0.033.

Conclusion- Hence, we conclude that intrathecal hyperbaric 0.75% ropivacaine provides satisfactory anaesthesia in comparison to bupivacaine with comparable onset, longer duration sensory blockade and faster motor regression while providing stable hemodynamics during the intraoperative period in patients scheduled for lower limb surgeries.

Keywords: hyperbaric, ropivacaine, bupivacaine, fentanyl, lower limb surgeries, spinal anaesthesia.

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Dedicated

to

my family

&

Teachers

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INTRODUCTION

Subarachnoid block [SAB] has gained popularity among anaesthesiologists as a mode of anesthesia for lower limb surgeries because of the ease of administration, maintenance of consciousness and spontaneous respiration, adequate muscle relaxation along with benefit of prolonged post operative analgesia. It is a preferred technique over general anaesthesia due to its benefits of lower operative costs, reduced incidence of major perioperative complications like deep vein thrombosis, pulmonary embolism, respiratory complications, decreased stress response to surgery, decreased intraoperative blood loss and substantial pain in early post operative period.[1] Thus SAB has always remained the preferred choice of anesthesia for lower limb surgeries.

However, SAB is associated with adverse effects such as - hypotension, bradycardia, inadequate or failed block, postdural puncture headache, backache, urinary retention, meningitis etc. [2]

Various local anaesthetic (LA) agents have been employed for spinal anaesthesia (SA).

LA work by blocking voltage gated sodium channels causing a conformational change in the receptors which obstructs the electrical transmission across the nerve ending.

The clinically useful local anaesthetic agents are mainly of two broad categories. Agents having ester link between the aromatic portion and the intermediate chain, which are referred to as amino esters. These include procaine, chloroprocaine and amethocaine. While the one with an amide link between the aromatic end and the intermediate chain are referred to as amino amides which include lignocaine, mepivacaine, prilocaine, etidocaine, bupivacaine and ropivacaine. Due to their distinct structures, amino amides are chemically more stable. Esters are easily hydrolyzed in plasma by the enzyme cholinesterase and are relatively unstable in solution, whereas the amide compounds undergo enzymatic degradation in the liver.[3]

For an anesthesiologist, the clinically important properties which impact their choice of LA agents include drug potency, time of onset of sensory block (SB) and motor block (MB), degree of muscle relaxation and duration of SB and MB. Sympathetic fibres are most easily blocked, requiring the least concentration of LA to block neuronal transmission. Sympathetic blockade usually reaches a higher dermatome in contrast to SB and MB. In sensory blockade, temperature (cold) and pain (pinprick), are blocked first which is mediated by Aδ and C fibers, followed by loss of sensation to touch and proprioception which are mediated by Aϑ and Aβ fibers. Finally motor function is blocked which is carried by Aα fibers.

The local anesthetics were first used in the late 18th century. It started with use of cocaine which resulted in many fatalities. Thus various LA drugs were studied in 19th century. Drugs like prilocaine and lidocaine were used as LA for many years until bupivacaine was introduced into clinical practice in 1963.[4] Since then, bupivacaine has established itself ubiquotously as an intrathecal LA drug. It is a long acting LA [1-butyl-2',6'pipecolxylidine] which was first synthesized in 1957 by Ekenstan in Sweden, after which it underwent various trials and eventually achieved acceptance in virtually every area of local anaesthesia [LA] practice.[5]

Bupivacaine, just like the other LA drugs, acts by blocking voltage gated Na+ channels when they are in open state, in reversible and concentration dependent manner. This causes failure of nerve conduction, thus producing the resultant autonomic, sensory and motor blockade. Bupivacaine just like lidocaine, acts on cardiac Na+ channels and blocks them. This results in accumulation of the drug during diastole, prolongation of conduction pathway inducing re-entrant tracts causing arrhythmias [6].

Albright GA in 1979 published an article which stained the popularity of bupivacaine. He reported in his article about the six cardiac arrests which occurred after accidental intravascular injection of either

bupivacaine or etidocaine. This necessitated the development of a new local anesthetic drug- Ropivacaine. [7]

Ropivacaine, another long acting amide local anaesthetic, is almost similar in chemical structure when compared to bupivacaine. It was synthesized from its congener molecule propivacaine as a pure S (-) enantiomer. Compared to bupivacaine which had butyl group on its tertiary nitrogen atom, ropivacaine has a propyl group in its structure. This causes shortening of the carbon chain on tertiary nitrogen which renders ropivacaine less lipid soluble. This results in lesser drug causing penetration into large myelinated motor fibers and giving it the property of more selective sensory blockade.

Ropivacaine shows lower tendency to bind to myocardial Na+ and K+ channels, leading to minimal effect on myocardial electrical conduction and contractility as compared to bupivacaine.[6] Due to less lipid solubility and stereoselective structure, ropivacaine has significantly higher threshold for cardiotoxicity and CNS toxicity than bupivacaine. Thus ropivacaine was introduced in clinical practice with the claim to be less cardiotoxic than bupivacaine.[8] Initially ropivacaine was available in isobaric forms with different concentrations which soon made its place into the arena of regional anaesthesia. However, due to unpredictable spread of isobaric ropivacaine its use as an intrathecal anaesthetic agent became limited.

Based on the findings that ropivacaine in its hyperbaric formulations produced a more consistent block than the plain one, studies compared 0.5% hyperbaric ropivacaine (made by adding glucose) with 0.5% hyperbaric bupivacaine and revealed that ropivacaine provides shorter sensory and motor blockade and with reduced potency when compared with bupivacaine.[9] In a trial involving lower limb surgeries the duration of SB with ropivacaine 15mg was found similar to bupivacaine 10 mg with a significantly shorter MB. [10] It was also proposed that on a milligram for milligram basis, the potency of

ropivacaine relative to bupivacaine is two- thirds with regard to SB and half with regard to MB .[11]

Since hyperbaric preparations of ropivacaine 0.75% were unavailable, few studies compared reconstituted hyperbaric 0.75% ropivacaine (prepared by adding glucose to isobaric ropivacaine) with hyperbaric 0.5% bupivacaine for clinical efficacy under spinal anaesthesia in lower limb surgeries and revealed that hyperbaric 0.75% ropivacaine is a better alternative to hyperbaric 0.5% bupivacaine with better block characteristics and hemodynamic stability.[12]

Recently, hyperbaric preparation of 0.75% ropivacaine equipotent to 0.5% hyperbaric bupivacaine has been commercially launched after conducting a successful phase 3 multicentric trial where 0.75% hyperbaric ropivacaine has shown comparable efficacy and better safety profile in comparison with 0.5% hyperbaric bupivacaine when used by intrathecal route.

To enhance the blockade of intrathecal drugs, addition of intrathecal opioids as adjuvant to LA has become a favorable and preferred method in spinal anesthesia. They intensify the SB without increasing the sympathetic blockade and also diminish the side effects associated with high dose of LA.[13] It has also been observed that they are associated with decreased pain scores and reduced analgesic requirements in the post operative period making intrathecal opioids popular adjuvants for lower limb surgeries.

Lately, few studies investigating the efficacy of 0.75% hyperbaric ropivacaine in spinal anesthesia have shown contrasting results, and there is limited research on efficacy of 0.75% hyperbaric ropivacaine with fentanyl in spinal anaesthesia. Thus, a prospective randomized controlled study was conducted to differentiate between the anaesthetic efficacy of equipotent doses of hyperbaric 0.75% ropivacaine and 0.5% hyperbaric bupivacaine in combination with fentanyl for spinal anaesthesia in lower limb surgeries.

AIMS AND OBJECTIVES

To compare the efficacy and safety, in terms of onset and duration of sensory and motor block, of hyperbaric 0.75% ropivacaine versus hyperbaric 0.5% bupivacaine in combination with fentanyl in spinal anaesthesia for lower limb surgeries.

REVIEW OF LITERATURE

Karl August Bier introduced spinal anesthesia in 1898. Spinal anaesthesia also called subarachnoid block or intrathecal block is a type of regional anesthesia where the LA is injected into subarachnoid space through a very fine 23G/ 26G needle (preferably dura splitting needle due to lesser incidence of dural puncture headache). This results in blockade of sensory fibers and motor fibers along with sympathetic blockade. Regional anaesthesia has advantage over general anaesthesia that it is less toxic. Thus after the discovery of SA, various drugs were studied to be used as LA, which were given intrathecally to improve the quality of block. [14]

Itinerary of Local Anesthetic drugs in the history of spinal anesthesia

The journey of Intrathecal local anaesthetics started with James Leonard Corning, who described the use of cocaine (the only naturally occurring local anesthetic) for spinal anesthesia.[15] Case reports of fatalities with cocaine started surfacing during its use as an intrathecal drug. Various ester LA were manufactured during the time frame from 1891 to 1930, i.e. benzocaine, eucaine, holocaine, tropocaine, orthoform, and tetracaine. Certain amino amide LA were also synthesized during 1898 to 1972 which included efocaine, nirvaquine, chloroprocaine, mepivacaine, cinchocaine, lidocaine, procaine, prilocaine, bupivacaine, etidocaine, and articaine.[16]

Subsequently, Braun in 1905 successfully performed spinal anesthesia using procaine. Sise in 1935 used tetracaine as LA for subarachnoid block. Later in mid 19th century, lidocaine was studied and synthesized. In 1949, Gordh first used lidocaine as intrathecal drug and it remained a popular LA for around two decades.[17] In early 1960's case reports of cardiotoxicity and neurotoxicity associated with lidocaine started catching everyone's attention. This initiated the persuit for the synthesis of a drug which would be a safe alternative to lidocaine and

which could provide effective muscle relaxation and along with sensory blockade. Thus bupivacaine came into limelight with Emblem being the first one to use it as an intrathecal drug in 1966.[17]

From there on, bupivacaine (in various concentrations) has been used drug as the most common LA for both spinal anesthesia and topical anesthesia.

Bupivacaine

Bupivacaine is an amide LA with a piperidine ring structure due to which bupivacaine along with the other congener drugs like mepivacaine, ropivacaine etc are known as pipecholylxylidines. With molecular weight of 288 and pKa of 8.1, bupivacaine offers moderate onset and longer duration of action. The partial coefficient of 560 renders bupivacaine highly lipid soluble with a relative solubility of 1000. Mechanism of action is by Na+ channel inhibition just like other LA, but bupivacaine has comparatively higher affinity for cardiac Na+ channels which are inhibited for a relatively longer time and the drug dissociates very slowly from these channels causing increased risk of conduction blocks, re-entrant pathways and fatal arrhythmias. It has an inhibitory effect on cyclic AMP resulting in vasodilation which is refractory to standard resuscitation guidelines. Due to this vasodilatory effect, bupivacaine is rapidly absorbed. Its metabolism occurs in liver (dealkylation) to form pipecolic acid and pipecolylxylidine with half life ($t_{½}$) of 160 mins.[18,19]

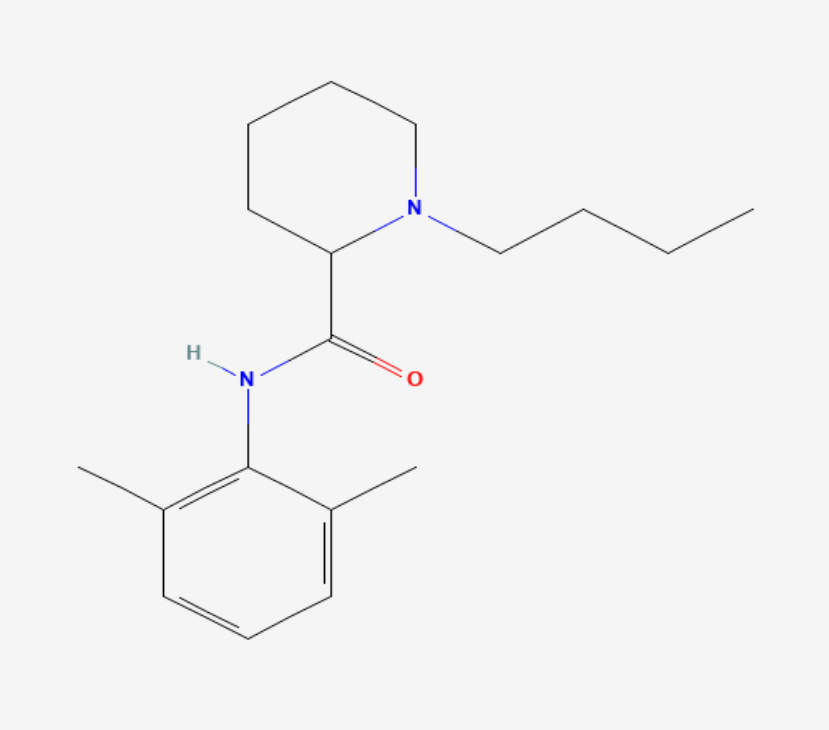


Figure 1: Structure of Bupivacaine.

Source- National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 2474, Bupivacaine. https://pubchem.ncbi.nlm.nih.gov/compound/Bupivacaine.[20]

Ropivacaine

Ropivacaine is a pure S(-)enantiomer. It is almost similar in structure to bupivacaine except for the functional group on the piperidine nitrogen atom which is propyl group in case of ropivacaine while butyl group in case of bupivacaine. Ropivacaine is structurally shorter in length due to the less number of carbon atoms as compared to bupivacaine which makes the former less lipid soluble. Its toxicity profile was studied extensively before the drug was introduced into the market in 1996.[16]

It is an amide LA with a molecular weight of 274 and is 94% protein bound with long duration of action. It has a pKa of 8.1 offering it moderate onset of action. The partial coefficient of 230 renders it less lipid soluble with a relative lipid solubility of 300. It acts by inhibition of Na+ channels just like other LA, with very less affinity for cardiac Na+ channels and early dissociation from the channels avoiding any cadiac side-effects as seen in bupivacaine. It has a bimodal action on blood

vessels causing vasodilation at clinical doses and vasoconstriction at subclinical doses. Its metabolism occurs in liver (aromatic hydroxylation) to form 3-hydroxy ropivacaine which gets excreted in urine with a half life ($t_{½}$) of 120 mins.[18,19]

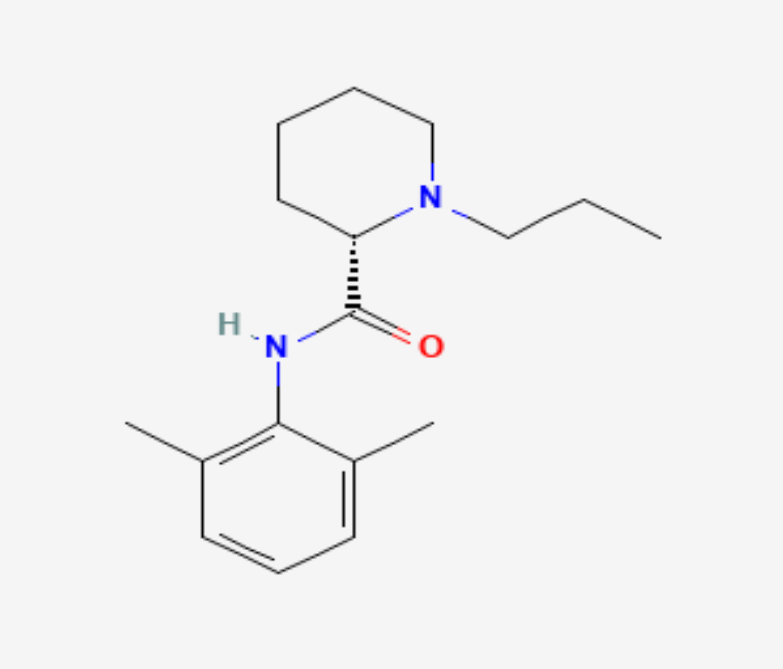


Figure 2: Structure of Ropivacaine.

Source- National Center for Biotechnology Information (2024). PubChem Compound Summary for CID 175805, Ropivacaine. https://pubchem.ncbi.nlm.nih.gov/compound/Ropivacaine.[21]

Being less lipophilic, ropivacaine penetrates less into large myelinated motor fibers like Aβ which are involved in motor function. It has selective action on the pain transmitting Aδ and C fibres. It has been found that in equipotent doses the degree of motor blockade is less pronounced with ropivacaine. Thus ropivacaine shows more selective sensory blockade than bupivacaine which is lipophilic and produce profound sensory and motor block.[22]

Furthermore, it was observed that using hyperbaric LA solutions in comparison to isobaric solutions, favored a reasonable and predictable spread along with providing a clinically useful blockade (given by

duration of blockade at T10 dermatome) with a rapid sensory regression and recovery from MB .[23]

Ropivacaine: Then and Now

After the introduction of bupivacaine in the market, there was increased usage of the drug in SA and many incidences of CNS as well as CVS toxicity were reported. A number of experiments were conducted to identify the mechanism of this toxicity and for better understanding of the action of LA. This led to identification of optically active isomers of the mepivacaine family and selection of ropivacaine to be used intrathecally to produce subarachnoid block.[16]

Ropivacaine has been used in epidural anaesthesia for caesarean section and hip and lower limb surgeries; for SA in place of bupivacaine and in peripheral nerve blocks for both surgical anaesthesia and postoperative pain management.[24] Isobaric solutions of ropivacaine were studied for many years but it was observed that higher doses of isobaric ropivacaine were required in order to provide block characteristics comparable to bupivacaine without producing any significant advantage.[25]

Eventually available solutions of ropivacaine were made hyperbaric and used to study the effect of its 0.5% hyperbaric formulations in comparison to hyperbaric bupivacaine 0.5% in hip and lower limb surgeries. Dar FA et al in 2015 published a study where hyperbaric solution of ropivacaine 0.5% was prepared aseptically by mixing 0.75% isobaric ropivacaine (5 ml) with 25% dextrose (2 ml) and 0.5 ml sterile water at room temperature. Thus making a total volume of 7.5ml with final glucose concentration of 6.6% in hyperbaric ropivacaine solution. A total of 3ml of the prepared drug was given. The prospective study was done among 200 patients aged 40-75 years randomly divided into two groups. The mean onset of SB at T-10 level (6 ± 1.3 min vs. 3 ± 1.1 min; $P < 0.001$) and MB (13 ± 1.6 min vs. 9 ± 1.3 min; $P < 0.001$) was significantly slower in ropivacaine group as compared to bupivacaine group. Sensory block (SB) was defined as complete regression till S1 dermatome which was significantly shorter with ropivacaine group (160 ± 12.9 min) than with bupivacaine group (260 ±

16.1 min; P < 0.001). Motor block (MB) was also shorter in the ropivacaine group compared to bupivacaine group (126 ± 9.2 min vs. 174 ± 12.6 min; P<0.001). The intraoperative quality of anaesthesia was similar in both groups (P=0.4). Thus it was concluded in the study that hyperbaric bupivacaine used intrathecally has a faster onset of sensory block and longer analgesia in comparison to hyperbaric ropivacaine.[26]

Ghimire et al in 2019 compared the effectiveness of hyperbaric 0.5% bupivacaine (3ml) with glucose 8% and hyperbaric 0.5% ropivacaine (3ml) with glucose 8.33% in 60 patients. It was concluded that the time to onset of maximum sensory block level was faster in bupivacaine (9.10±3.90min) than in ropivacaine (10.87±5.37min) and statistically not significant. The time required for five segment regression was faster in ropivacaine (116.00±29.72min) than bupivacaine (143.50±18.76min) and the time required for regression till S2 level was faster in ropivacaine (154.00±27.84min) than bupivacaine (186.00±18.73min). The time required for onset of maximum motor blockade was faster with bupivacaine (8.70±3.19min) as compared to ropivacaine (13.10±4.40min).Their final impression was that hyperbaric ropivacaine (3ml, 0.5%) provides a reliable subarachnoid block of shorter duration than hyperbaric bupivacaine (3ml, 0.5%) with stable hemodynamic parameters.[27]

Kharat et al in February 2021 studied the block characteristics using 4ml of each hyperbaric ropivacaine 0.5% and hyperbaric bupivacaine 0.5% in 70 patients undergoing elective lower abdominal, perineal and lower limb surgeries under spinal anesthesia. They used reconstituted drugs i.e. bupivacaine 5 mg/ml with glucose 80 mg/ml = 4 ml and ropivacaine 5 mg/ml with glucose 80 mg/ml = 4 ml. They found out that bupivacaine showed rapid onset of sensory block (p<0.05) and faster cephalic spread than ropivacaine. In this study both the study drugs obtained adequate motor block while the time required to achieve modified bromage score (MBS) 3 was not significant. Bupivacaine took significantly longer time for complete regression (P=0.0001). Hemodynamic parameters were statistically insignificant although the

diastolic and mean pressures were found to be on lower side in bupivacaine group ($p<0.05$). They concluded that 0.5% hyperbaric ropivacaine provided a comparable sensory block of shorter duration of action with less frequent episodes of hypotension as compared to hyperbaric 0.5% bupivacaine.[28]

Chatterjee et al reconstituted 0.75% hyperbaric ropivacaine with glucose 50% and compared its efficacy with hyperbaric 0.5% bupivacaine (total volume of 3ml of each drug) in 100 patients planned for lower limb surgery under SA. He observed that patients who received ropivacaine showed delayed onset and shorter duration of SB and MB when comparison to patients who received bupivacaine. Clinically, no significant difference was noticed in perioperative hemodynamics when comparing the two groups. This study observed that if hyperbaric ropivacaine is administered in equipotent doses, it produces analgesia and anesthesia which are of shorter duration when compared to hyperbaric bupivacaine.[29]

With the availability of commercial preparation of 0.75% hyperbaric ropivacaine in the market, it emerged as a popular interest of research.

In July 2023, Garaniya et al conducted a trial on sixty patients using 3ml of commercially available 0.75% hyperbaric ropivacaine and 3ml of commercially available 0.5% hyperbaric bupivacaine undergoing lower abdominal surgeries to differentiate the hemodynamic parameters, block characteristics and quality of anaesthesia. They found that, mean arterial blood pressure (MAP) significantly reduced during the initial 10 to 30 minutes post intrathecal injection of bupivacaine in comparison to ropivacaine. They noticed a significantly longer time in onset of sensory blockade with ropivacaine than with bupivacaine ($p <0.0001$). Ropivacaine took significantly longer time for maximal sensory blockade. Ropivacaine regressed faster to L1 and MBS 0 than bupivacaine($P= 0.001$). They concluded that ropivacaine offered comparable muscle relaxation with hemodynamically stable profile and safety with faster recovery from both sensory and motor blockade.[30]

Gohil et al in October 2023 studied the similar dose (3ml) of the two drugs but had contrasting results. They enrolled sixty patients, planned

for lower limb orthopedic surgery. Using hyperbaric 0.75% ropivacaine (3ml) and hyperbaric 0.5% bupivacaine (3 mL) intrathecally, they found out that ropivacaine showed earlier onset of SB i.e. 2.6 ± 0.53 mins in comparison with bupivacaine i.e. 3 ± 0.56 mins with P<0.006. In this study, ropivacaine group showed faster regression to S1 dermatome i.e. 120.16 ± 7.73 mins in comparison to bupivacaine i.e. 180 ± 11.56 mins (P<0.0001). Ropivacaine group showed significantly faster regression of motor blockade 149.5 ± 8.64 mins than bupivacaine i.e. 210 ± 13.19 mins (P<0.0001). They concluded that ropivacaine 0.75% hyperbaric is a comparable substitute to bupivacaine 0.5% hyperbaric in patients planned for lower limb orthopedic surgery.[31]

Kalbande et al in March 2024 took 60 patients posted for elective infra-umbilical surgeries giving either 3mL 0.5% hyperbaric bupivacaine group or 3mL 0.75% hyperbaric ropivacaine. They found out that ropivacaine showed delayed onset for both sensory (defined as appearance of numbness and tingling in patient) and motor blockade (time till appearance of MBS grade 1) P<0.001. They studied two-segment sensory regression and found out that ropivacaine (91.12 ± 5.08 mins) regressed faster than bupivacaine (100.65 ± 6.87 mins). Similar results were found with motor blockade defined as complete motor regression to MBS 0. In this clinical trial, both the study groups showed comparable results when compared for duration of SB (defined as regression of SB till S1 dermatome). They concluded that equipotent doses of the two study drugs produced comparable block characteristics with ropivacaine being a safer alternative with earlier better motor-regression[32].

Role of opioids as adjuvants in SA

To further intensify the level of SB and for better analgesia, intrathecal opioids were introduced as adjuvants to spinal drugs. Intrathecal opioids are synergistic to LA as they produce similar effect by acting on different receptors. LA bind at nerve axon level while intrathecal opioids bind to opioids receptors located in laminae I and II at the spinal dorsal horn reducing nociceptive transmission.[33] They intensify the SB without increasing the sympathetic blockade and also diminish the side

effects associated with high dose of LA. They also help in prolonging the duration of postoperative analgesia and offer hemodynamic stability.[13] Amongst all opioids fentanyl is the most commonly used. Compared with I/V fentanyl, Intrathecal fentanyl decreased visceral and somatic pain and improved the quality of block. It has also been associated with reduced pain and analgesic requirements in post operative period making it popular for use as an adjuvant in SA. The near absence of depression of respiration with fentanyl (with permissible dose of 25 µgm) ,better pulmonary spirometric function and shorter hospitalization makes it an ideal drug for intrathecal use.[34]

Various studies have observed that intrathecal opioids have a synergistic effect when used with local anaesthetics in spinal anesthesia. Chaudhary et al (2014) enrolled 60 male patients of ASA I-III posted for TURP, where Group A (n=30) received intrathecal injection of isobaric ropivacaine 2 ml (0.75%) and Group B (n = 30) isobaric ropivacaine 1.8 ml (0.75%) with fentanyl 10 µg (0.2ml). The block characteristics, hemodynamic stability, and side effects were observed. Maximum level of SB was at T10 in group A and T9 in group B (P = 0.001). Duration of MB was longer in group B being 210.51 ± 61.25 min than in group A being 286.25 ± 55.65 min (P < 0.001). They concluded that addition of fentanyl to ropivacaine may offer the advantage of earlier regression of motor block and hemodynamic stability without any increase in the frequency of major side effects.[35]

To find out the clinical efficacy of intrathecal opioids when used along with hyperbaric solution of 0.75% ropivacaine, A Khunongbham K et al in 2016 performed a comparative double blinded randomized study on 60 patients posted for lower abdominal and lower limb surgeries. He reconstituted hyperbaric 0.75% ropivacaine and hyperbaric 0.5% bupivacaine solutions. 30 patients received hyperbaric 0.5% bupivacaine (2 ml) with fentanyl 0.4 ml and normal saline (0.25 ml) making a total volume of 2.65 ml while other 30 patients also received 2.65 ml of total drug i.e. ropivacaine 0.75% (2 ml) with fentanyl 0.4 ml, 0.2 ml of 50% dextrose and normal saline (0.05 ml). The spinal block characteristics and hemodynamic parameters were recorded and

statistically analyzed. The time to attain maximum level of SB (group R 9.10 ± 1.97 min; group B 9.17 ± 1.51min; P > 0.05) and median maximum extent (ropivacaine T6; bupivacaine T5; P > 0.05) was comparable in the two groups, but the mean duration of sensory block regression to S2 dermatome was significant (ropivacaine 157.44 ± 17.78 min; bupivacaine 180.60 ± 23.06 min; P < 0.001). The degree of MB was significant between the groups (ropivacaine 1.50 ± 0.82; bupivacaine 2.40 ± 0.49; P < 0.001). Patients who were administered ropivacaine, mobilized sooner (ropivacaine 115.47 ± 17.07 min; bupivacaine 154.60 ± 20.37 min; P < 0.001) . It was thus concluded that 15 mg of ropivacaine with fentanyl 20 µg was a better alternative to bupivacaine (heavy) 10 mg with better block characteristics and hemodynamic stability.[12]

Gupta et al in a recent study in February 2024 enrolled sixty adult patients posted for elective transurethral resection of prostate. They used 0.75% hyperbaric ropivacaine - 2.8mL plus fentanyl 15 mcg and 0.5% hyperbaric bupivacaine 2.8mL plus fentanyl 15 mcg. They analyzed that ropivacaine showed delayed onset of SB (defined as time to reach T10 dermatome) Ropivacaine= 5.38±0.62 mins and Bupivacaine=3.94±0.76 mins with P= 0.0001. The onset of MB (defined as complete motor blockade to MBS grade 3) in group R (7.51±1.43 mins) was delayed in comparison to group B (5.65±0.82 mins) with P= 0.0001. Group R showed better hemodynamics and lesser episodes of hypotension compared to bupivacaine. They concluded that 0.75% hyperbaric ropivacaine is a better option for in elderly patients scheduled for TURP as compared to 0.5% hyperbaric bupivacaine.[36]

Taken together, these studies suggest that hyperbaric 0.75% ropivacaine can be used as an alternative to hyperbaric 0.5% bupivacaine for SA. The use of hyperbaric ropivacaine 0.75% as intrathecal local anaesthetic agent for spinal anaesthesia may aid in early ambulation of patient with lesser haemodynamic instability and thus we planned to evaluate its blocking characteristics in patients posted for elective lower limb surgeries under SA.

MATERIALS AND METHODS

SOURCE OF DATA

A prospective, randomized, double-blind study was conducted in Department of Anesthesiology after approval from the Institutional Ethics Committee on 60 adult patients posted for lower limb surgeries under spinal anaesthesia. A written informed consent was obtained from all the patients included in the study.

METHOD OF COLLECTION OF DATA

Inclusion criteria:

1. Patients aged between 18-65 years of either gender scheduled for lower limb surgery under spinal anaesthesia.
2. American Society of Anaesthesiologists (ASA) grade I, II and III.

Exclusion criteria:

1. Patient refusal for subarachnoid block.
2. Allergy to local anaesthetic drugs or any history of anaphylactic reaction to the drugs used.
3. Frank coagulopathy evidenced by history and laboratory investigations.
4. Infection at injection site.
5. Patients with spinal deformities like kyphoscoliosis and scoliosis etc.
6. Patients with history of pre-existing neurological disease.
7. Non co-operative patients.
8. Patients with only one limb which is the operative limb.
9. BMI ≥ 35 kg/m^2

GROUP ALLOCATION:

Patients were randomly allocated to either of the two groups- Group R and B of 30 patients each by computer generated random numbers contained in sealed, sequentially numbered envelopes. The study was made double blind as the patient and the investigator were unaware of the nature of drug used. The name of the drug used was sealed in an envelope which was opened by the anaesthetist administering spinal anaesthesia and not involved in data collection.

Group R - Patients received 3ml of intrathecal drug which included 2.5ml of 0.75% hyperbaric ropivacaine and 25µg (0.5 ml) fentanyl.

Group B - Patients received 3ml of intrathecal drug which included 2.5ml of 0.5% hyperbaric bupivacaine and 25µg (0.5 ml) fentanyl.

METHODOLOGY

PREANAESTHETIC CHECK UP

Each patient included in this study underwent a preanaesthetic evaluation (PAC) one day prior to the planned surgery in which thorough history taking, general physical and systemic examination was done. PAC included any known drug allergies, prior surgical and anaesthetic exposure, and detailed systemic evaluation to rule out any cardiac, neurological, endocrine, hepatic or respiratory disorders. It was used as a tool to document patient's baseline vital parameters and all the necessary routine investigations which included hemogram, renal function tests, coagulation profile and chest X-ray. During the evaluation of the patients, they were explained about the study protocol and visual analogue scale (VAS) used to measure the post operative pain. A written informed consent was obtained from patient willing to participate in the study.

PREMEDICATION

All patients were instructed to follow the nil per oral guidelines and maintain ≥8 hours of fasting for solids and ≥2 hours of fasting for clear

fluids. Night before the surgery all patients received tablet alprazolam 0.25mg followed by tablet pantoprazole 40mg on the morning of surgery with sips of water. On arrival in preoperative area, I.V. access was established using 18G/20G cannula.

ANAESTHESIA TECHNIQUE

On arrival in the operating room (OR), the patients were positioned on the operating table in the supine position and monitored with continuous electrocardiography (ECG), cyclic noninvasive blood pressure (NIBP), and peripheral oxygen saturation (SpO2). Mean of three consecutive readings of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and SpO2 at one minute interval were recorded as baseline. All patients were administered 10 mL/kg of crystalloids intravenously before the onset of spinal anaesthesia.

The drug code was contained in a sealed envelope and 60 such envelopes were made for all the cases. Each envelope was opened by the designated anesthesiologist who loaded the mentioned drug in a 5cc syringe along with adjuvant (fentanyl). Under all aseptic precautions and with patients placed in sitting position, skin infiltration of L3-L4 interspace with 2ml of 2% lignocaine was performed followed by lumbar puncture at same interspace with a 26G Quincke's needle using a midline approach. Group R (30 patients) received 3ml of intrathecal drug which included 2.5ml of 0.75% hyperbaric ropivacaine and 25µg fentanyl and Group B (30 patients) received 3ml of intrathecal drug which included 2.5ml of 0.5% hyperbaric bupivacaine and 25µg fentanyl. The bevel of the needle was kept cranial during injection. After free flow of cerebrospinal fluid was verified, anaesthetic solution was injected at rate of 0.2ml/sec. Patients were immediately placed in supine position after the spinal anesthesia with OR table in neutral position. The drug used was decoded after the completion of study.

INTRAOPERATIVE ASSESSMENT

Immediately after the intrathecal injection (taken as 0 min) HR, SBP, DBP**,** MBP and SpO2 were recorded. Patients were assessed for the level of sensory block using a pinprick method with a sterile 26G needle pricked in mid clavicular line on either side. Level of sensory blockade was noted at 0 min, 2min, 4min, 6min, 8 min, 10 min, 15 min and thereafter every 15 minutes till two dermatome regression from maximum level of sensory block. The surgery was allowed to commence after sensory block reached T10. The degree of motor block in the lower limbs was assessed using a Modified Bromage Scale (MBS)[37] at 0 min, 2min, 4min, 6min, 8 min, 10 min, 15 min and thereafter every 15 minutes till onset of motor block.

Modified Bromage Scale[37] **–**

0= free movement of legs and feet

1= unable to raise the extended legs but able to flex knees with free movement of feet

2= unable to flex knees but with the free movement of feet

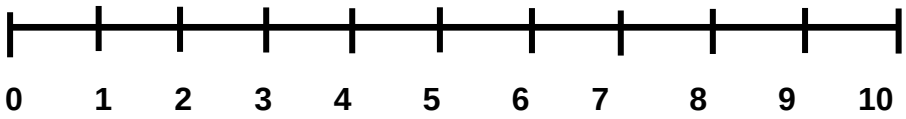
3= unable to move legs and feet.

Hemodynamic parameters were assessed at 0 min, 2min, 4min, 6min, 8 min, 10 min, 15 min and thereafter every 15 minutes throughout the surgery. Hypotension, defined as a fall in systolic blood pressure >20% from the baseline was treated with IV injection of ephedrine 6 mg and IV fluids. A fall in heart rate <50 beats/min was considered as bradycardia and treated with injection atropine 0.6 mg IV. After completion of the surgery the hemodynamic parameters as well as the level of sensory and motor block were documented and then the patient was shifted to Post Anaesthesia Care Unit (PACU).

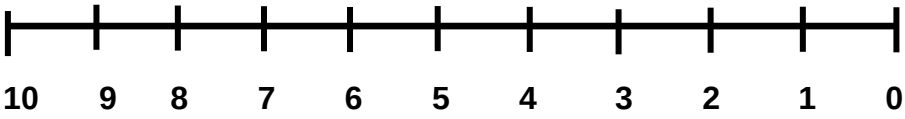
POSTOPERATIVE ASSESSMENT

Upon shifting the patient in post anesthesia care unit, the HR, MAP, SBP, DBP, SpO_2, VAS and MBS of the patient were recorded. The MBS was recorded every 30 minutes till complete recovery of motor block. Haemodynamic parameters were assessed hourly. Pain was

assessed using visual analogue scale (VAS) - it's a 10 point scale wherein 0 indicates no pain and 10 indicates worst imaginable pain. It was assessed hourly for 6 hours post-operatively.



No pain **Worst pain**



Worst pain **No Pain**

Time to first analgesic demand was noted when VAS was more than 4 and patients were given Inj. Tramadol 100mg I.V. slow. Hospital protocols were followed for pain management. Any side effects (discomfort, nausea, vomiting, shivering, pruritis, hypotension and bradycardia) in six hours postoperatively were recorded and any intervention required was noted. All the parameters were noted by the assessor who was blinded to the nature of intrathecal drug administered. Patients with failed spinal anaesthesia and subsequent conversion to general anaesthesia were excluded from the study.

OUTCOMES OF THE STUDY

PRIMARY OUTCOME

Duration of sensory block (minutes)- The duration of sensory block was defined as the period from intrathecal injection till two dermatome regression from maximum (highest) level of sensory block (in minutes).

SECONDARY OUTCOMES

1. The onset of sensory block (minutes) - The onset of sensory block was defined as the time between injection of intrathecal anaesthetic and the absence of pain at T10 dermatome assessed by pinprick test.
2. Maximum (highest) level of sensory block
3. Time required to achieve maximum (highest) level of sensory block (minutes)
4. Time required for onset of motor block (minutes) - Time for onset of motor block was defined as the period from intrathecal injection till the MBS is grade 3.
5. Total duration of motor block (minutes) – It was defined as the period from intrathecal injection till complete motor block recovery (MBS- grade 0).
6. Duration of analgesia – It was defined as period from onset of sensory block to the time for first rescue analgesic demand or when the VAS was ≥4.
7. Episodes of hypotension and bradycardia.

POWER AND SAMPLE SIZE

The formula used is as under:

$n = (\sigma_1^2 + \sigma_2^2)\ (Z_\alpha + Z_\beta)^2/(\ m_1 - m_2)^2$

Where,

Z_α = Value of standard normal variate corresponding to α level of significance (1.96)

Z_β = The standard normal deviate for desired power (0.842)

m = Average

σ = Standard deviation

Assumptions:

From the Pilot study

Mean Group (m_1) = 67.5

Mean Group (m_2) = 56.25

Coefficient of variation = 150%

Standard deviation Group (σ_1) = 15
Standard deviation (σ_2) = 14.36

With the above assumptions the sample size for 95% confidence level & 80% power works out 27 in each group. So we took 30 each cases.

STATISTICAL ANALYSIS:

The continuous variables like age, BMI, duration of surgery, onset and duration of sensory and motor block were described in terms of mean ± standard deviation (SD).

For categorical variables like gender, ASA grade, episodes of hypotension and bradycardia, maximum (highest) level of sensory block, data was described in terms of frequencies (number of cases) and relative frequencies (percentages).
To determine whether the data were normally distributed, a Kolmogorov-Smirnov test was used.

For comparison of continuous data between the two study groups i.e. age, BMI, duration of surgery student t-test was used.

Z-test was used for comparison of data like amount of vasopressor needed to treat hypotension, total amount of I.V. fluids administered, time to onset of sensory block, time to maximum (highest) sensory level, duration of sensory block, time to onset of motor block, total duration of motor block, duration of analgesia.

For comparing categorical data like gender, comorbidities, ASA grade, episodes of hypotension and bradycardia, maximum (highest) level of sensory block, the side effects associated with the study drugs, Chi square ($\chi 2$) test was performed.

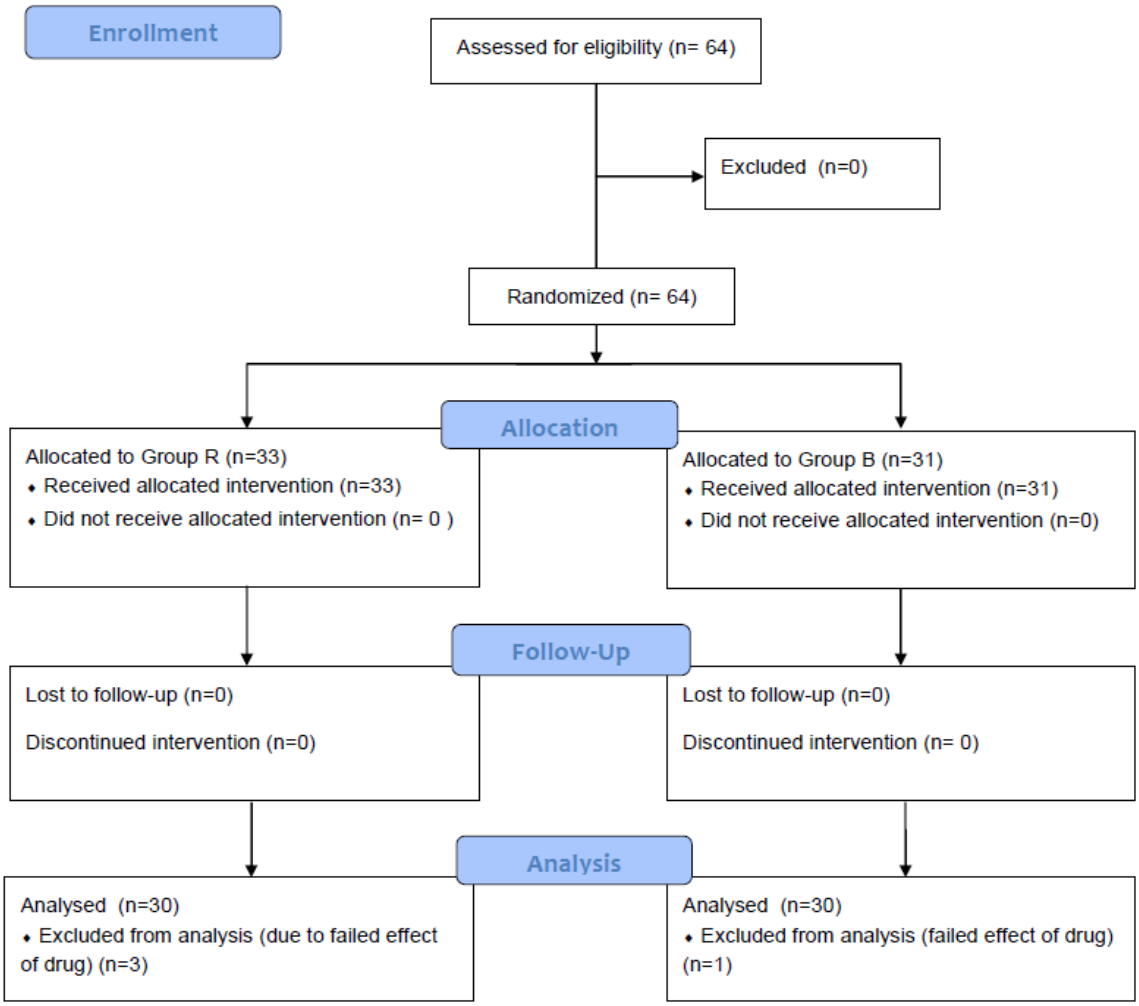
A probability value (p value) less than 0.05 was considered statistically significant.

All statistical calculations were done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Window.

OBSERVATION AND RESULTS

This prospective randomized controlled trial was conducted on 60 patients from January 2023 to December 2023. Patients were divided into two groups - Group R (Ropivacaine) and Group B (Bupivacaine).

FIGURE 3: CONSORT Flow diagram of the study.


Enrollment
Assessed for eligibility (n= 64)
Excluded (n=0)
Randomized (n= 64)
Allocation
Allocated to Group R (n=33)
• Received allocated intervention (n=33)
• Did not receive allocated intervention (n= 0)
Allocated to Group B (n=31)
• Received allocated intervention (n=31)
• Did not receive allocated intervention (n=0)
Follow-Up
Lost to follow-up (n=0)
Discontinued intervention (n=0)
Lost to follow-up (n=0)
Discontinued intervention (n= 0)
Analysis
Analysed (n=30)
• Excluded from analysis (due to failed effect of drug) (n=3)
Analysed (n=30)
• Excluded from analysis (failed effect of drug) (n=1)

A total of 64 patients were enrolled for the study according to the inclusion criteria. None of the patients were excluded during the enrollment phase. Sixty four patients were randomly allocated to either of the group by computer generated random number and sixty patients were analyzed after excluding four patients due to failed drug effect while conducting the study. They were analyzed using SPSS 21 version statistical program for Microsoft Windows. [Figure 3]

Demographic data was similar in both the groups

TABLE 1: COMPARISON OF STUDY GROUPS ACCORDING TO AGE.

	GROUP R		GROUP B		T	p-value
	Mean	SD	Mean	SD		
Age	37.70	15.89	43.23	12.68	-1.491	0.141

The mean age of patients in group R was 37.70 ± 15.89 years and 43.23 ± 12.68 years in group B. There was no statistical difference in the age distribution among two groups (p>0.05). [Table1, figure4]

FIGURE 4: COMPARISON OF STUDY GROUPS ACCORDING TO AGE.

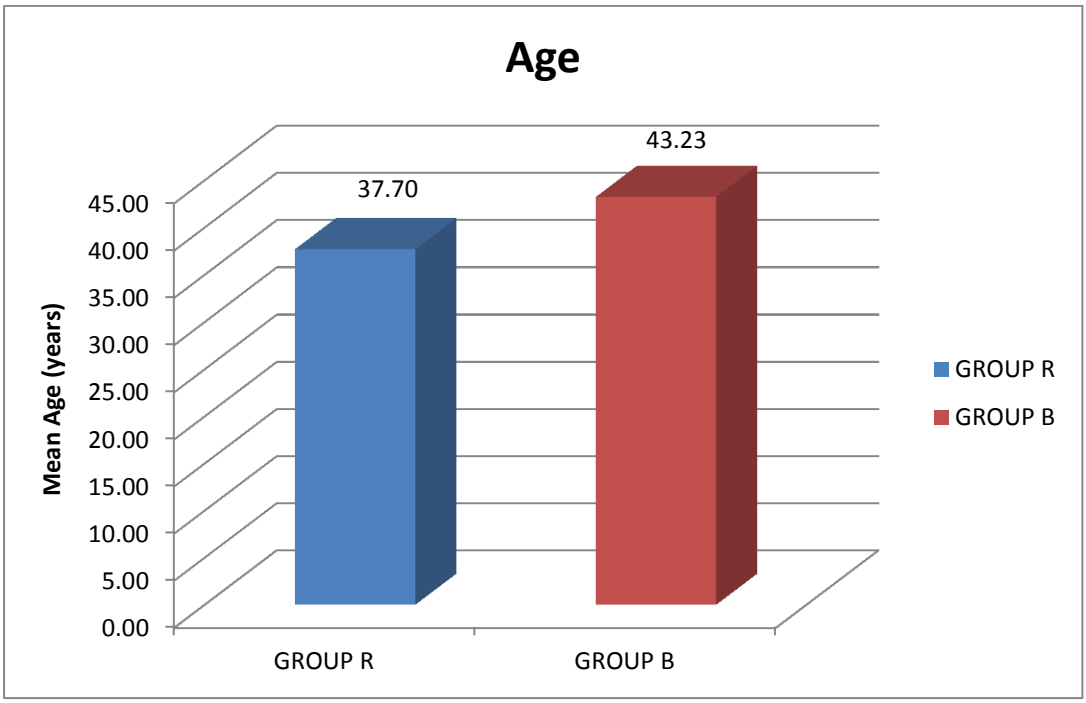


TABLE 2: COMPARISON OF STUDY GROUPS ACCORDING TO GENDER DISTRIBUTION.

		GROUP R		GROUP B		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Sex	F	3	10.0%	4	13.3%	7	0.162	0.688
	M	27	90.0%	26	86.7%	53		

In Group R, 10.0% of the patients were females and 90.0% were males whereas, in Group B, 13.3% were females and 86.7% were males. The difference between both groups was comparable statistically concerning sex distribution, with a p-value of 0.688. [Table2, figure5]

FIGURE 5: COMPARISON OF STUDY GROUPS ACCORDING TO GENDER DISTRIBUTION.

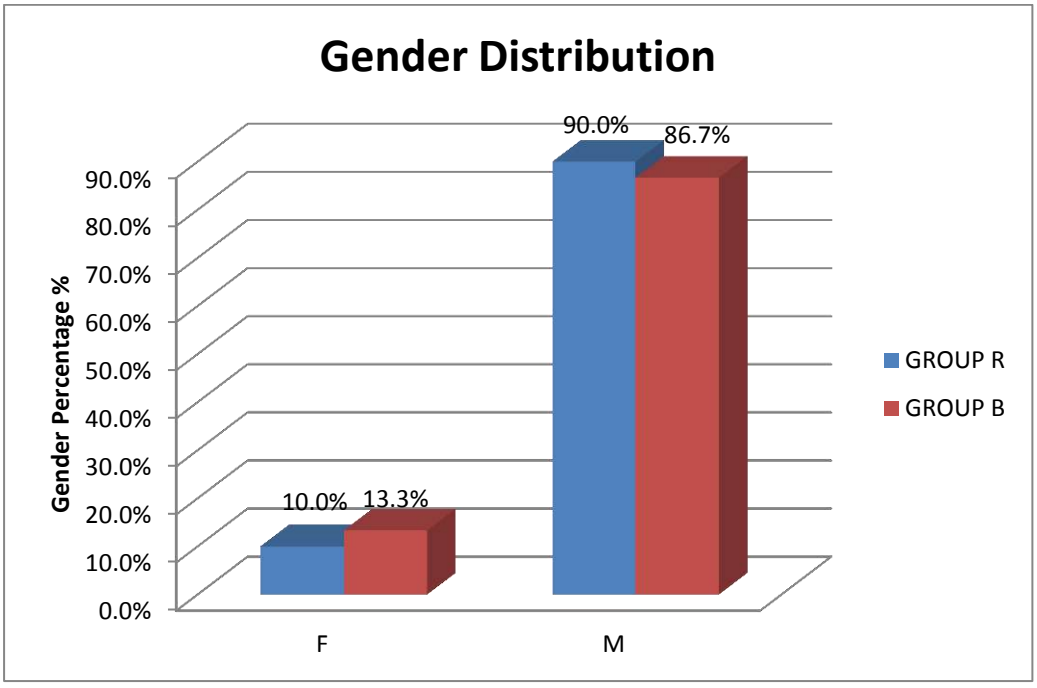


TABLE 3: COMPARISON OF STUDY GROUPS ACCORDING TO BASAL METABOLIC INDEX (BMI).

	GROUP R		GROUP B		T	p-value
	Mean	SD	Mean	SD		
BMI(kg/m^2)	25.47	4.11	26.45	3.19	-1.027	0.309

The mean BMI of patients in Group R was 25.47 ± 4.11 kg/m^2 and 26.45 ± 3.19 kg/m^2 in group B .There was no statistically significant difference (p>0.05) of mean BMI distribution among patients in both the groups (p value of 0.309). [Table3, figure6]

FIGURE 6: COMPARISON OF STUDY GROUPS ACCORDING TO BASAL METABOLIC INDEX (BMI).

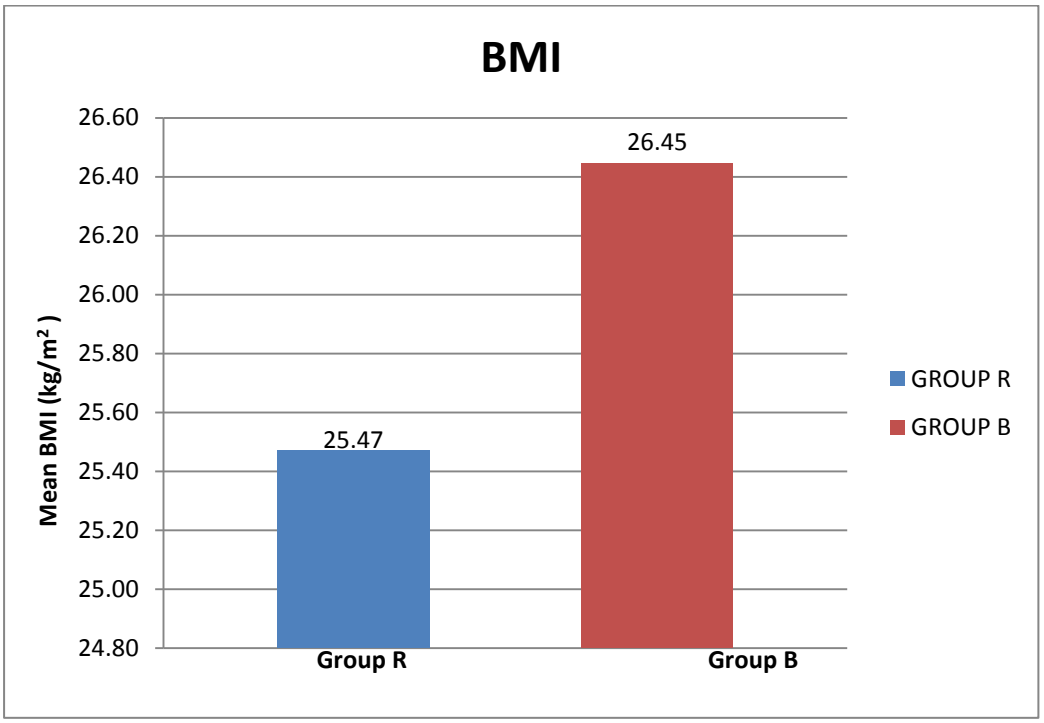


TABLE 4: COMPARISON OF STUDY GROUPS ACCORDING TO ASA GRADE.

		GROUP R		GROUP B		Total	Chi-square value	p-value
ASA Grade	I	17	56.7%	12	40.0%	29	1.7	0.427
	II	9	30.0%	13	43.3%	22		
	III	4	13.3%	3	10.0%	9		

In group R 56.7%, 30.0% and 13.3% of the patients were ASA I, II and III respectively whereas in group B 40.0%, 43.3% and 10.0%of the patients were ASA I, II and III respectively. Both of the groups were comparable in view of ASA grading and there was no statistically significant difference (p >0.05) between both the groups. [Table4, figure7]

FIGURE 7: COMPARISON OF STUDY GROUPS ACCORDING TO ASA GRADE.

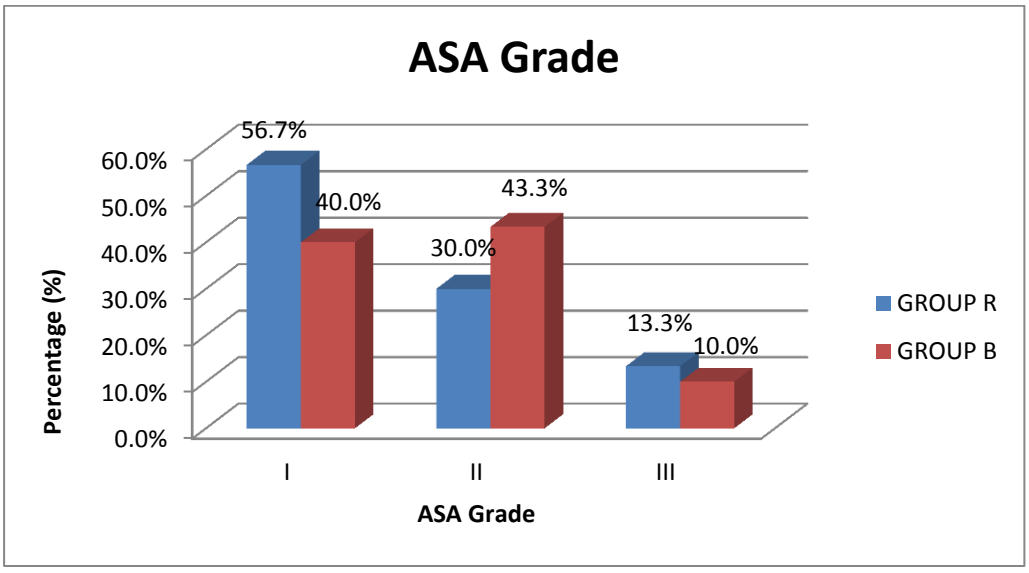


TABLE 5: COMPARISON OF STUDY GROUPS ACCORDING TO COMORBIDITIES PRESENT.

		GROUP R		GROUP B		Total	Chi-square value	p-value
Comorbidities	CAD, Hypertension	0	0.0%	1	3.3%	1	13.233	0.278
	CKD, Hypertension	0	0.0%	1	3.3%	1		
	CLD, Diabetes Mellitus Type 2	0	0.0%	1	3.3%	1		
	Diabetes Type 2	1	3.3%	3	10.0%	4		
	HCV +	2	6.7%	0	0.0%	2		
	Hypertension	0	0.0%	3	10.0%	3		
	Hypertension, Diabetes Type 2	2	6.7%	1	3.3%	3		
	Hypertension, Diabetes Type 2, CKD	0	0.0%	1	3.3%	1		
	None	23	76.7%	17	56.7%	40		
	Obese class 1	1	3.3%	1	3.3%	2		
	Overweight	0	0.0%	1	3.3%	1		
	Uncontrolled Hypertension	1	3.3%	0	0.0%	1		
Total		30	100.0%	30	100.0%	60		

The group R was distributed as 23.3% patients with comorbidities and 76.7% with no comorbidities while in group B, 43.3% patients had some comorbidity and 56.7% had no comorbidities. Both the groups were comparable in view of prevalence of comorbidities and there was no statistically significant difference ($p > 0.05$) between both the groups. [Table5, figure8]

FIGURE 8: COMPARISON OF STUDY GROUPS ACCORDING TO COMORBIDITIES PRESENT.

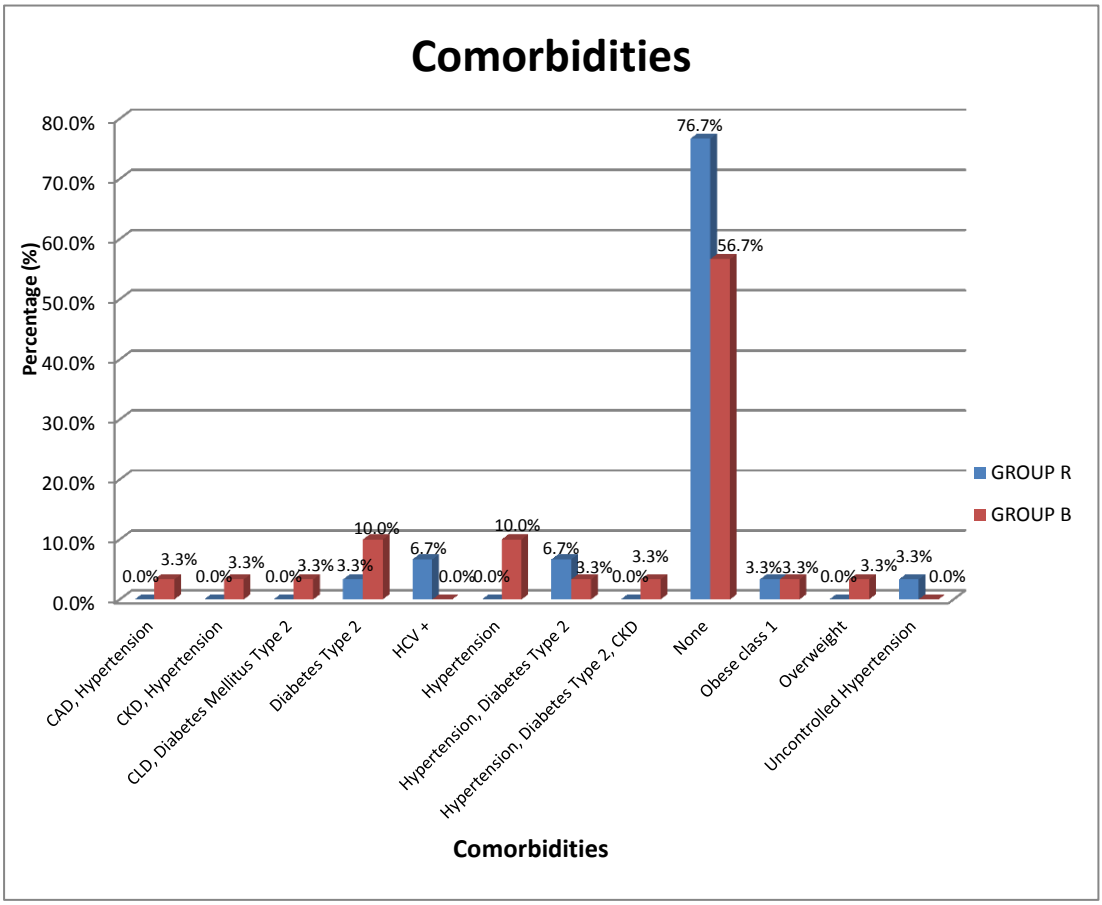


TABLE 6: COMPARISON OF STUDY GROUPS ACCORDING TO DURATION OF SURGERY (IN MINUTES)

	GROUP R		GROUP B		t	p-value
	Mean	SD	Mean	SD		
Duration of Surgery	66.70	38.88	69.33	33.19	-0.282	0.779

The duration of surgery was 66.70 ± 38.88 mins and 69.33 ± 33.19 mins in group R and group B respectively. The difference between both the study groups was statistically insignificant with p-value of 0.779. [Table6, figure9]

FIGURE 9: COMPARISON OF STUDY GROUPS ACCORDING TO DURATION OF SENSORY BLOCK (IN MINUTES)

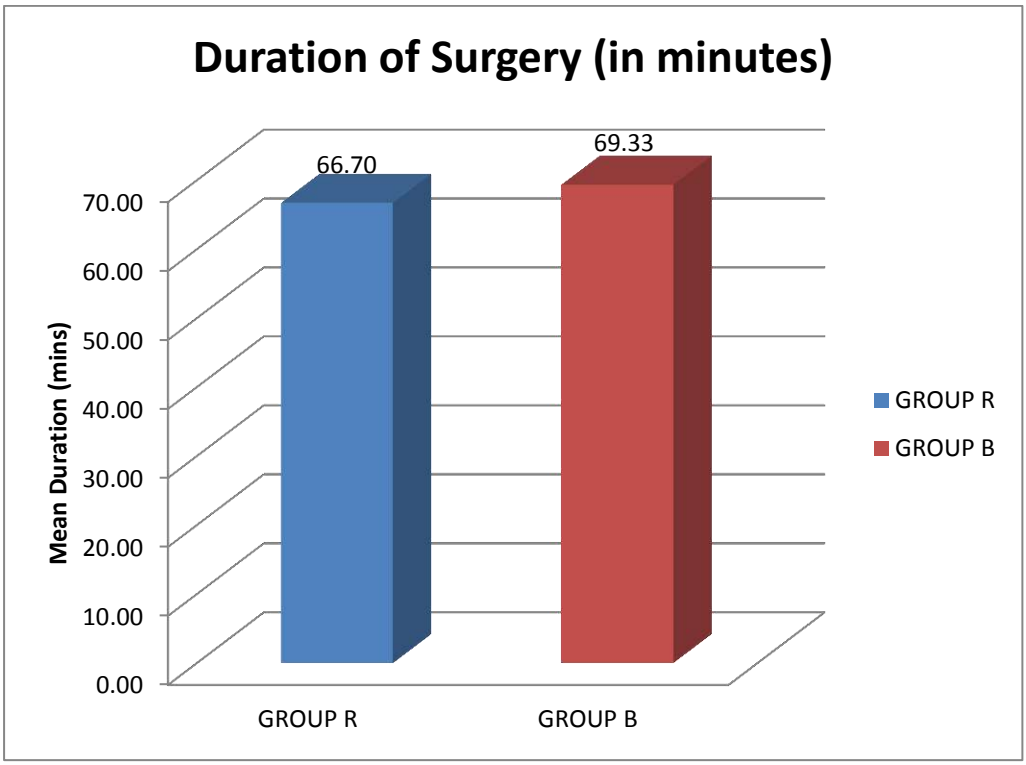


TABLE 7: COMPARISON OF STUDY GROUPS ACCORDING TO TOTAL AMOUNT OF I.V. FLUIDS ADMINISTERED (ML)

	GROUP R		GROUP B		Z	p-value
	Mean	SD	Mean	SD		
Total amount of I.V. fluids administered (ml)	1206.67	415.17	1381.67	402.68	-1.831	0.067

There was no statistically significant difference for the total amount of I.V. fluids administered (ml) to the patients between the two groups ($p>0.05$). [Table 7]

TABLE 8: COMPARISON OF STUDY GROUPS ACCORDING TO DURATION OF SENSORY BLOCK (IN MINUTES)

	GROUP R		GROUP B		Z	p-value	Difference		95% Confidence Interval of the difference	
	Mean	SD	Mean	SD			Mean	Std. Error	Lower	Upper
Duration of sensory block (in minutes)	99.27	11.79	85.17	19.19	-3.415	0.001	14.10	4.11	5.87	22.33

The duration of sensory block (defined as two dermatome regression from the highest level of sensory block) was 99.27 ± 11.79 mins and 85.17 ± 19.19 mins in group R and group B respectively. The difference between both the study groups was statistically significant with p-value of 0.001. [Table 8, figure10]

FIGURE 10: COMPARISON OF STUDY GROUPS ACCORDING TO DURATION OF SENSORY BLOCK (IN MINUTES)

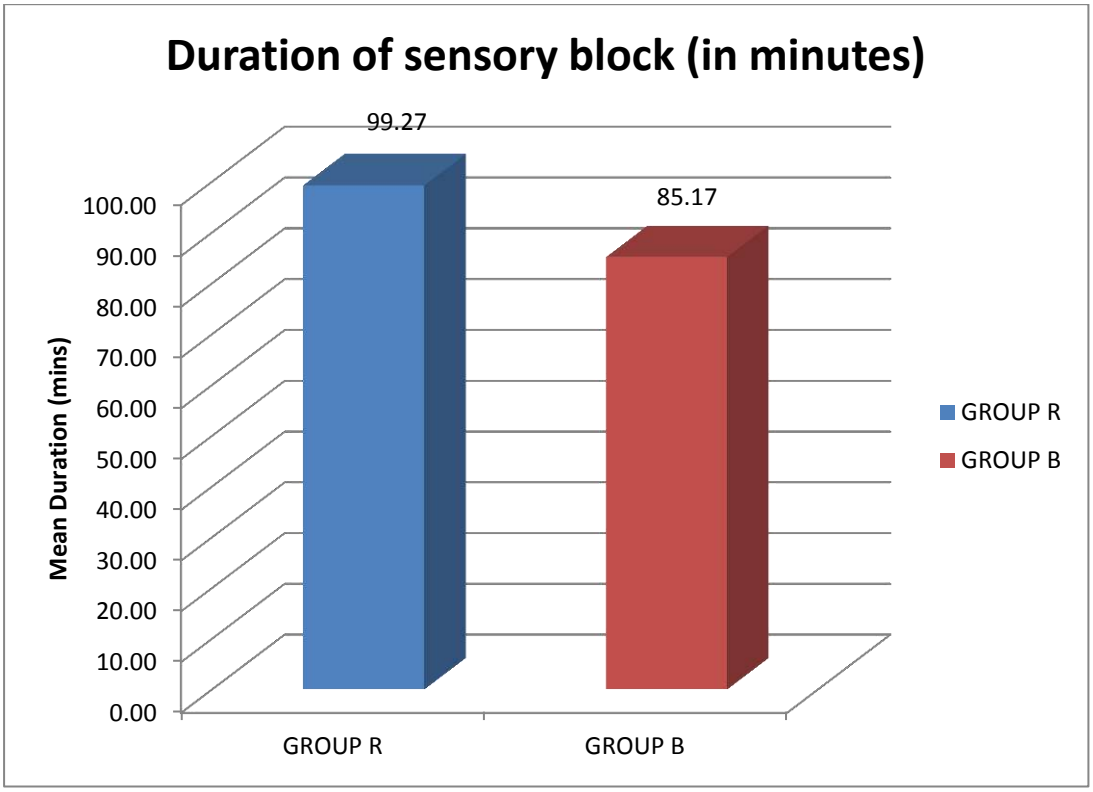


TABLE 9: COMPARISON OF STUDY GROUPS ACCORDING TO ONSET OF SENSORY BLOCK (IN MINUTES)

	GROUP R		GROUP B		Z	p-value	Difference		95% Confidence Interval of the difference	
	Mean	SD	Mean	SD			Mean	Std. Error	Lower	Upper
Time to onset of sensory block (in minutes)	6.30	3.66	7.00	5.37	-0.237	0.812	-0.70	1.19	-3.07	1.67

The onset of sensory block was 6.30 ± 3.66 mins and 7.00 ± 5.37 mins in group R and group B respectively. The difference between both the study groups was statistically insignificant with p-value of 0.812. [Table9, figure11]

FIGURE 11: COMPARISON OF STUDY GROUPS ACCORDING TO ONSET OF SENSORY BLOCK (IN MINUTES)

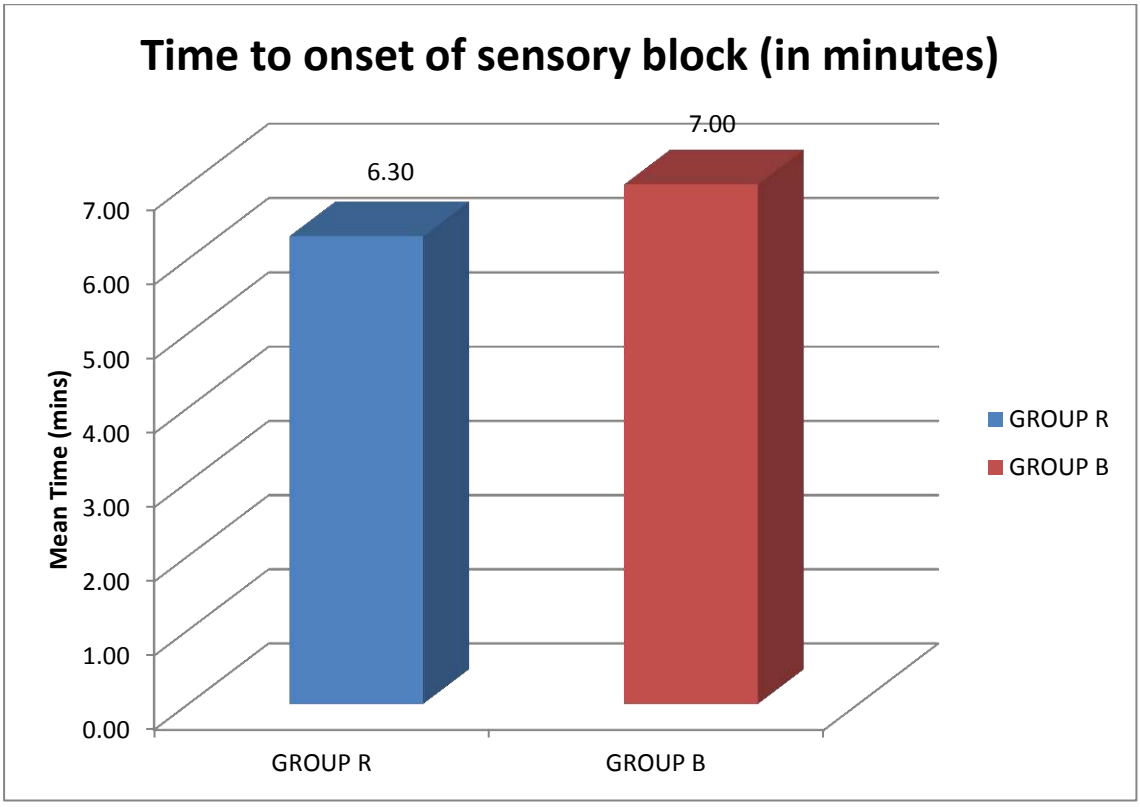


TABLE 10: COMPARISON OF STUDY GROUPS ACCORDING TO MAXIMUM (HIGHEST) SENSORY LEVEL ATTAINED

		GROUP R		GROUP B		Total	Chi-square value	p-value
Maximum sensory level attained	T3	1	3.3%	2	6.7%	3	7.056	0.216
	T4	10	33.3%	5	16.7%	15		
	T5	0	0.0%	4	13.3%	4		
	T6	8	26.7%	11	36.7%	19		
	T8	6	20.0%	5	16.7%	11		
	T10	5	16.7%	3	10.0%	8		
Total		30	100.0%	30	100.0%	60		

The highest (maximum) level of sensory block in group R was T3, T4, T6, T8 in 3.3%, 33.3%, 26.7% and 20.0% respectively. In Group B, the highest level was T3, T4, T5, T6 in 6.7%, 16.7%, 13.3%, 36.7% respectively. Therefore, the highest level of sensory block attained was comparable in both the groups with p >0.05. [Table 10, figure 12]

FIGURE 12: COMPARISON OF STUDY GROUPS ACCORDING TO MAXIMUM (HIGHEST) SENSORY LEVEL ATTAINED

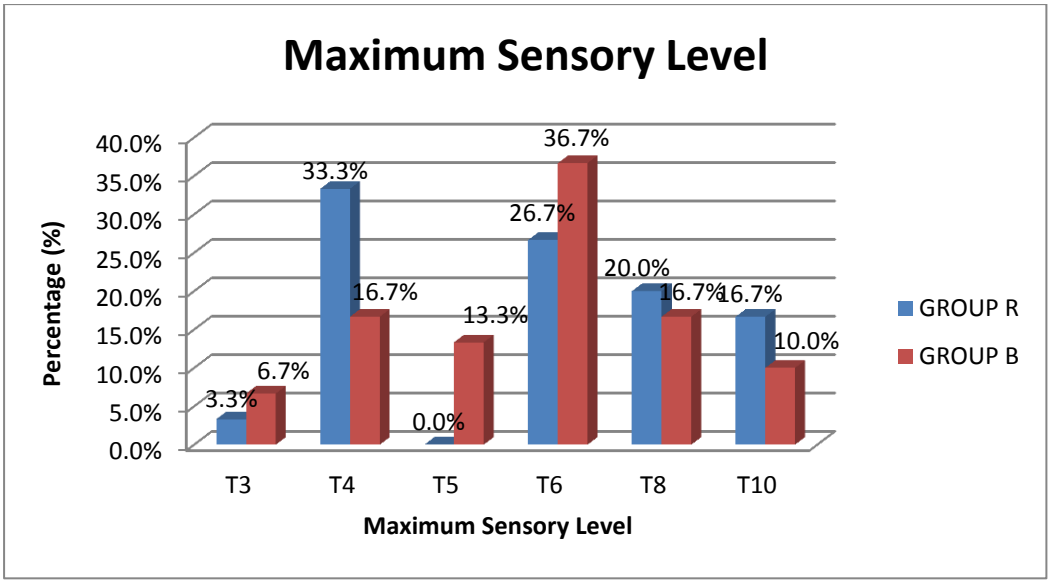


TABLE 11: COMPARISON OF STUDY GROUPS ACCORDING TO TIME REQUIRED TO ACHIEVE MAXIMUM (HIGHEST) LEVEL OF SENSORY BLOCK

	GROUP R		GROUP B		Z	p-value	Difference		95% Confidence Interval of the difference	
	Mean	SD	Mean	SD			Mean	Std. Error	Lower	Upper
Time to maximum (highest) sensory level (in minutes)	13.97	7.11	16.90	10.05	-0.960	0.337	-2.93	2.25	-7.43	1.57

The time required to reach maximum (highest) sensory level in group R was 13.97 ± 7.11 mins while in group B was16.90 ± 10.05 mins. The difference between both the study groups was found to be statistically insignificant for this variable as the p-value was >0.05. [Table11, figure13]

FIGURE 13: COMPARISON OF STUDY GROUPS ACCORDING TO TIME REQUIRED TO ACHIEVE MAXIMUM (HIGHEST) LEVEL OF SENSORY BLOCK

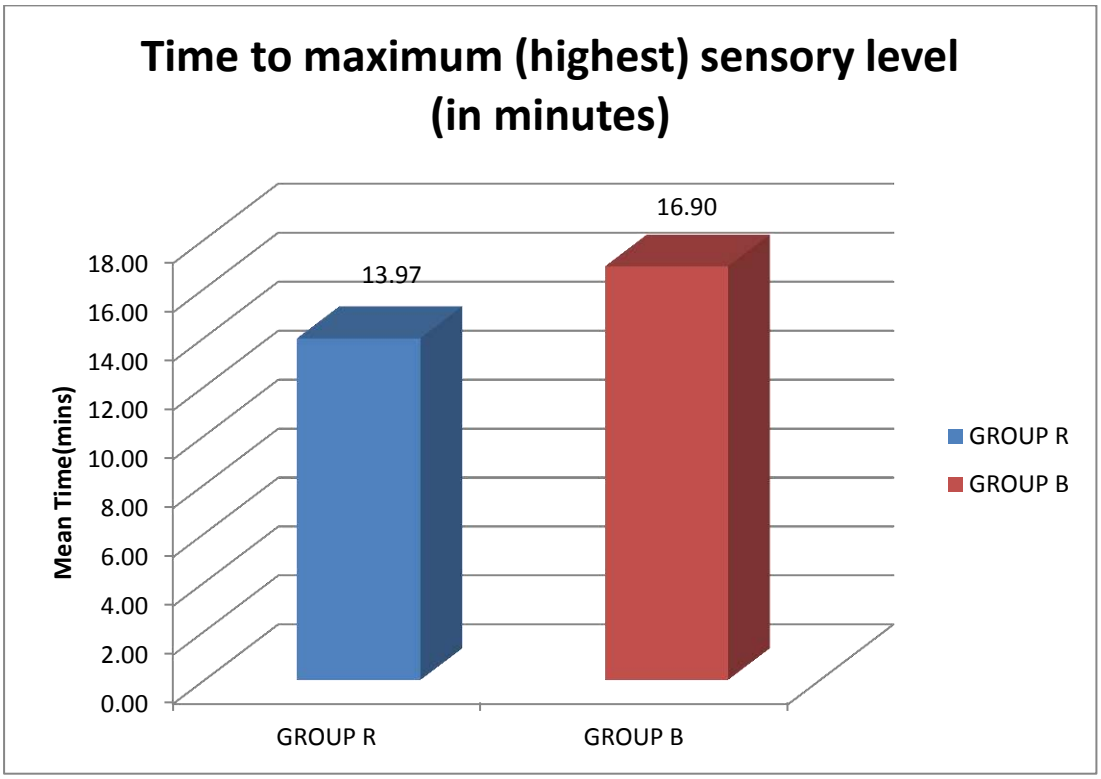


TABLE 12: COMPARISON OF STUDY GROUPS ACCORDING TO TIME REQUIRED FOR ONSET OF MOTOR BLOCK (MINUTES)

	GROUP R		GROUP B		Z	p-value	Difference		95% Confidence Interval of the difference	
	Mean	SD	Mean	SD			Mean	Std. Error	Lower	Upper
Time to onset of motor block (in minutes)	6.03	4.22	5.73	5.30	-0.560	0.576	0.30	1.24	-2.18	2.78

The time to onset of motor block (in minutes) was relatively more in Group R (6.03 ± 4.22 mins) than in group B (5.73 ± 5.30 mins). The difference between both the study groups was statistically insignificant with a p-value of 0.576. [Table12, figure14]

FIGURE 14: COMPARISON OF STUDY GROUPS ACCORDING TO TIME REQUIRED FOR ONSET OF MOTOR BLOCK (MINUTES)

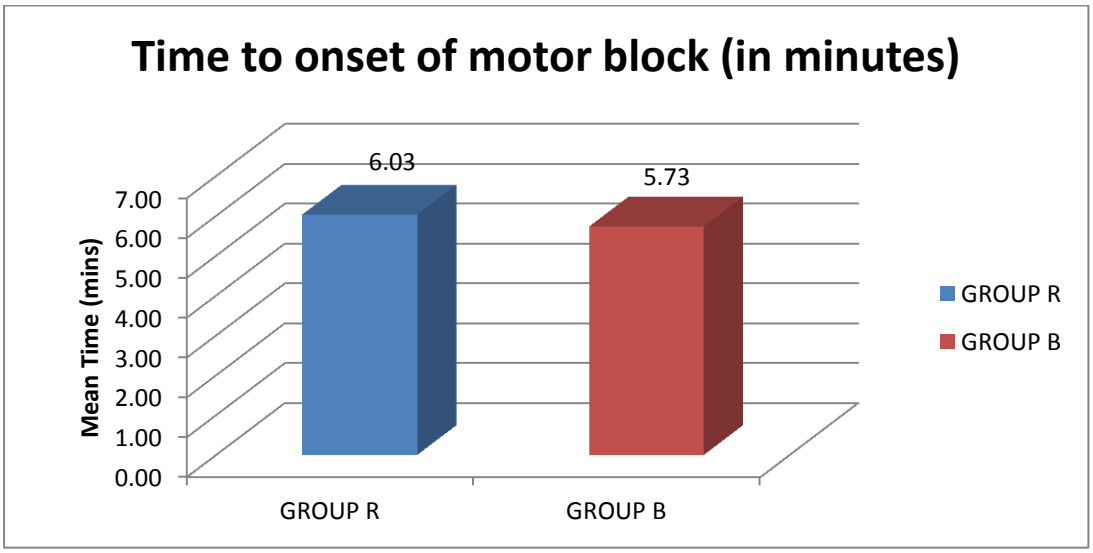


TABLE 13: COMPARISON OF STUDY GROUPS ACCORDING TO DURATION OF MOTOR BLOCK (MINUTES)

	GROUP R		GROUP B		Z	p-value	Difference		95% Confidence Interval of the difference	
	Mean	SD	Mean	SD			Mean	Std. Error	Lower	Upper
Total duration of motor block (in minutes)	175.90	40.81	205.07	57.17	-1.947	0.052	-29.17	12.82	-54.84	-3.50

The total duration of motor block (in minutes) was relatively less in Group R (175.90 ± 40.81 mins) than in group B (205.07 ± 57.17 mins). The difference between both the study groups was statistically insignificant with a p-value of 0.052. [Table13, figure15]

FIGURE 15: COMPARISON OF STUDY GROUPS ACCORDING TO DURATION OF MOTOR BLOCK (MINUTES)

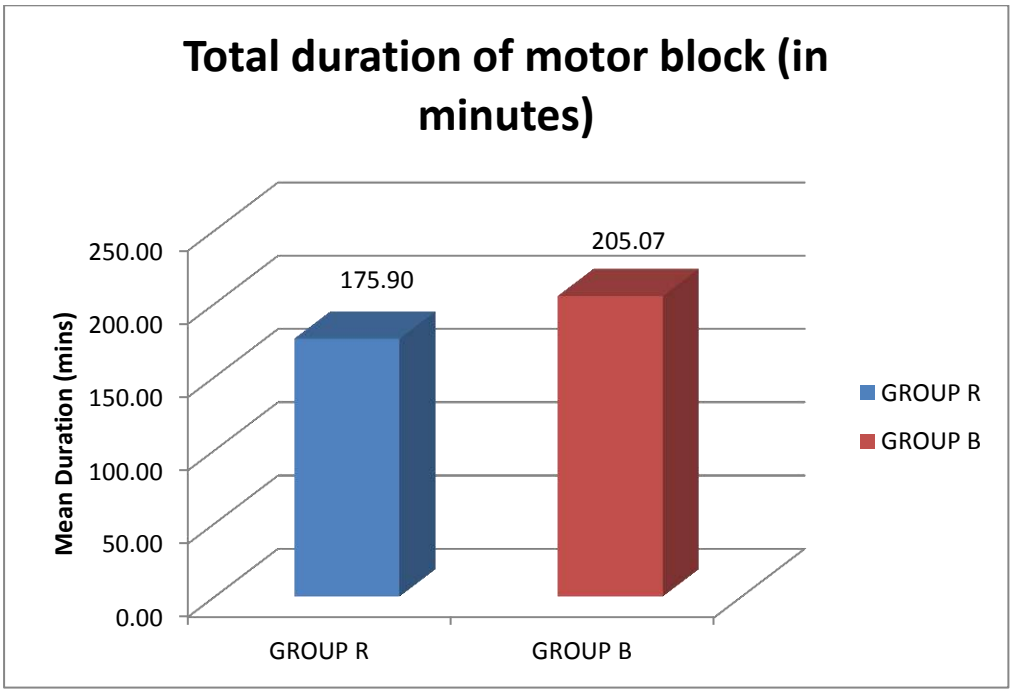


TABLE 14: COMPARISON OF STUDY GROUPS ACCORDING TO DURATION OF ANALGESIA (FIRST RESCUE ANALGESIC IN MINUTES)

	GROUP R		GROUP B		Z	p-value	Difference		95% Confidence Interval of the difference	
	Mean	SD	Mean	SD			Mean	Std. Error	Lower	Upper
Duration of analgesia (in minutes)	264.33	46.72	300.73	62.85	-2.487	0.013	-36.40	14.30	-65.02	-7.78

The mean duration of analgesia was defined as time from onset of sensory block to the time for first rescue analgesic demand or VAS ≥4. It was significantly lower in the Group R (264.33 ± 46.72 mins), than Group B (300.73 ± 62.85 mins). The difference between the two study groups was statistically significant with a p-value of 0.013. [Table14, figure16]

FIGURE 16: COMPARISON OF STUDY GROUPS ACCORDING TO DURATION OF ANALGESIA (FIRST RESCUE ANALGESIC IN MINUTES)

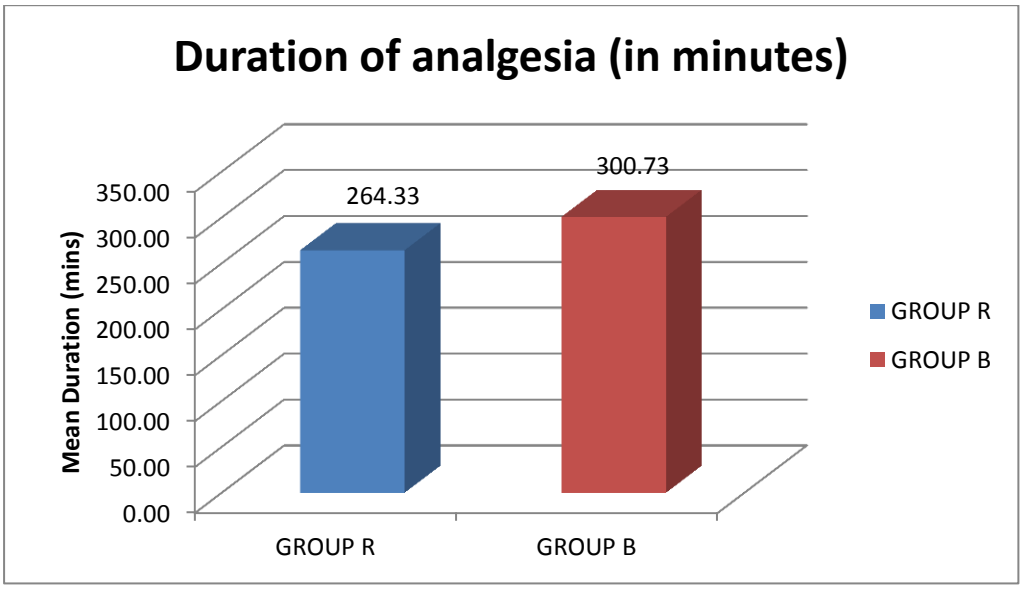
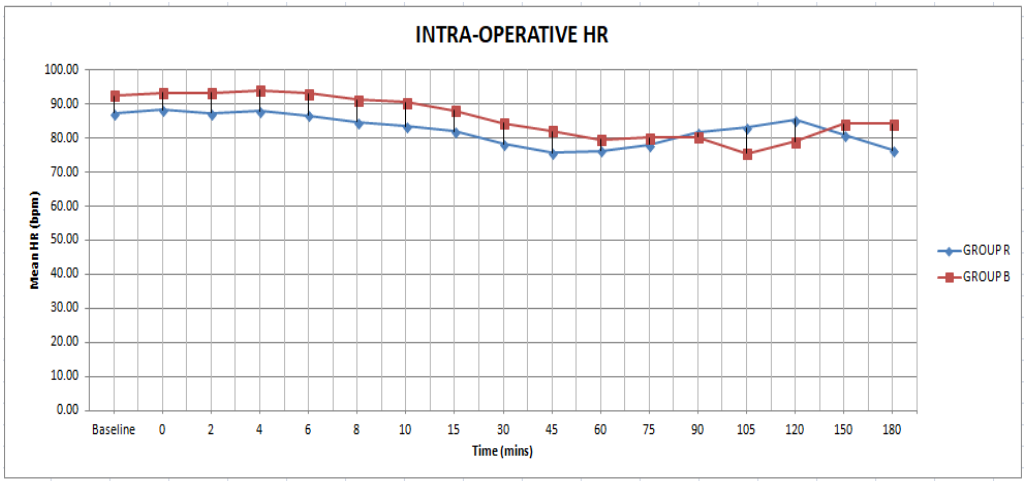
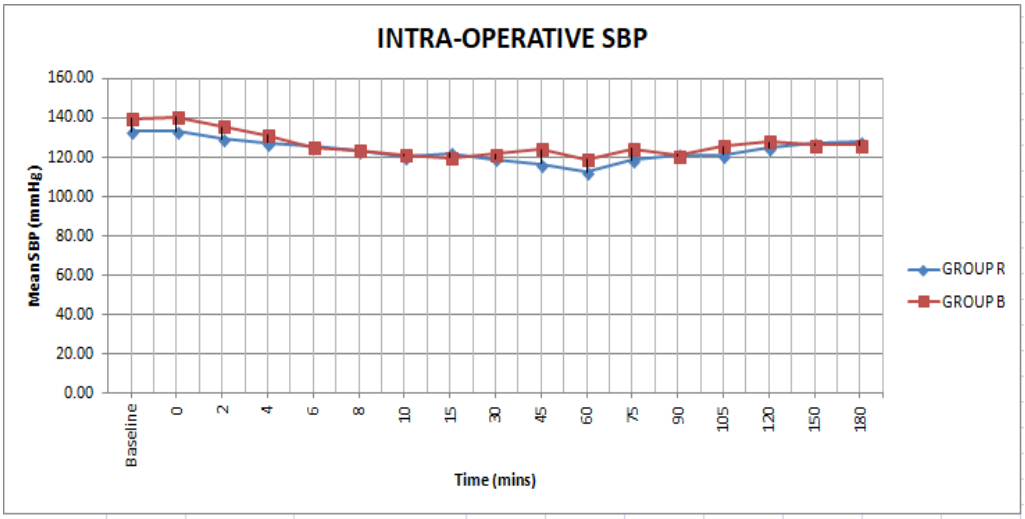


FIGURE 17: TRENDS OF INTRA-OPERATIVE HR VALUES IN BOTH GROUPS



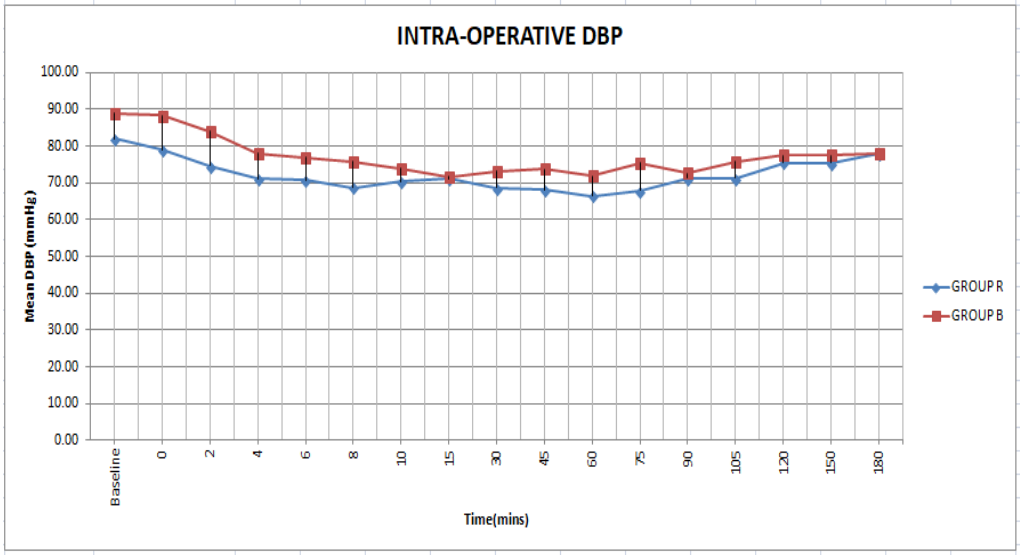
There was no statistically significant difference between the intra-operative HR values of the patients between both the groups (p>0.05). [Figure17]

FIGURE 18: TRENDS OF INTRA-OPERATIVE SYSTOLIC BLOOD PRESSURE (SBP) VALUES IN BOTH GROUPS



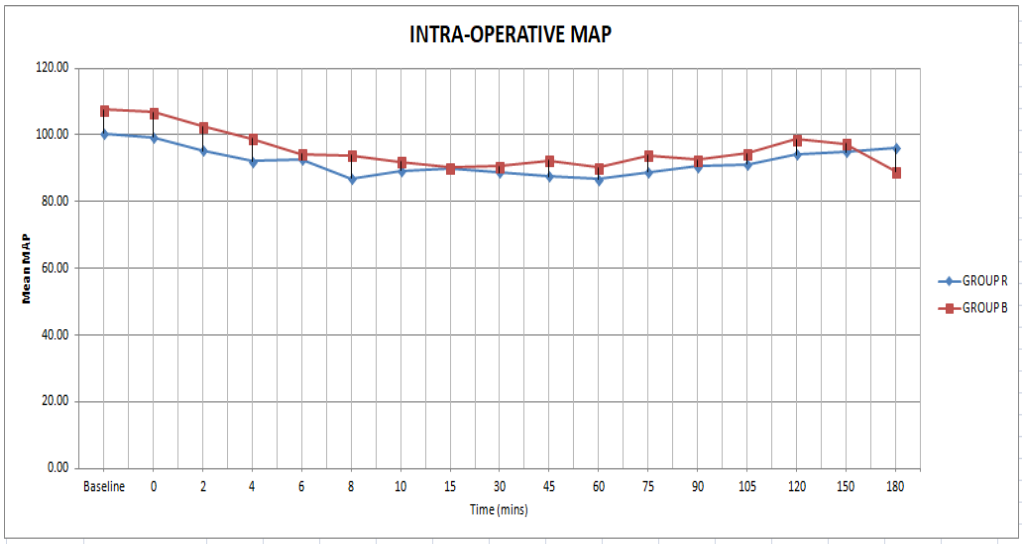
There was no statistically significant difference in SBP at all times intraoperatively in both the groups (p>0.05). [Figure18]

FIGURE 19: TRENDS OF INTRA-OPERATIVE DIASTOLIC BLOOD PRESSURE (DBP) VALUES IN BOTH GROUPS



There was no statistically significant difference between the intra-operative diastolic blood pressure (DBP) values of the patients between both the groups (p>0.05). [Figure 19]

FIGURE 20: TRENDS OF INTRA-OPERATIVE MEAN ARTERIAL PRESSURE (MAP) VALUES IN BOTH GROUPS



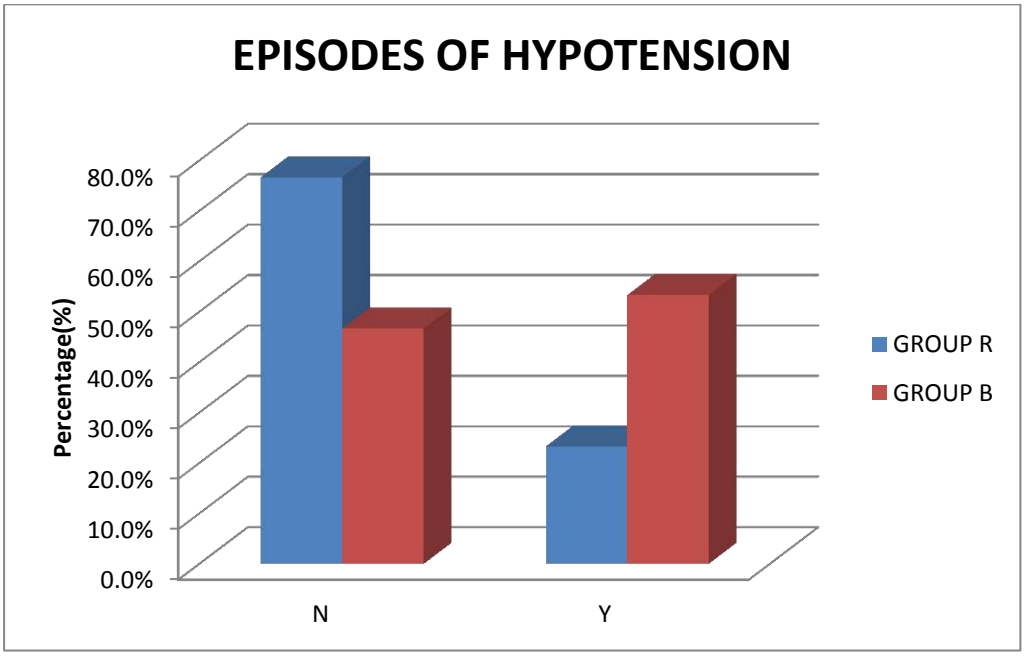
There was no statistically significant difference between the intra-operative mean arterial pressure (MAP) values of the patients between both the groups (p>0.05). [Figure 20]

TABLE 15: COMPARISON OF OCCURANCE OF EPISODES OF INTRAOPERATIVE BRADYCARDIA AND HYPOTENSION

		GROUP R		GROUP B		Total	Chi-square value	p-value
Episodes of Hypotension (Y/N)	N	23	76.7%	14	46.7%	37	5.711	0.033
	Y	7	23.3%	16	53.3%	23		
Episodes of Bradycardia	N	30	100.0%	30	100.0%	60	0.000	1.000
	Y	0	0.0%	0	0.0%	0		

Intraoperative hypotension i.e. fall in SBP ≥20% from baseline was observed in 23.3% patients in ropivacaine group while it occurred in 53.3% patients in bupivacaine group. The difference in incidence was statistically significant with p = 0.033. No episode of intraoperative bradycardia was observed in either of the groups. [Table 15, Figure 21]

FIGURE 21: COMPARISON OF OCCURANCE OF EPISODES OF INTRAOPERATIVE BRADYCARDIA AND HYPOTENSION



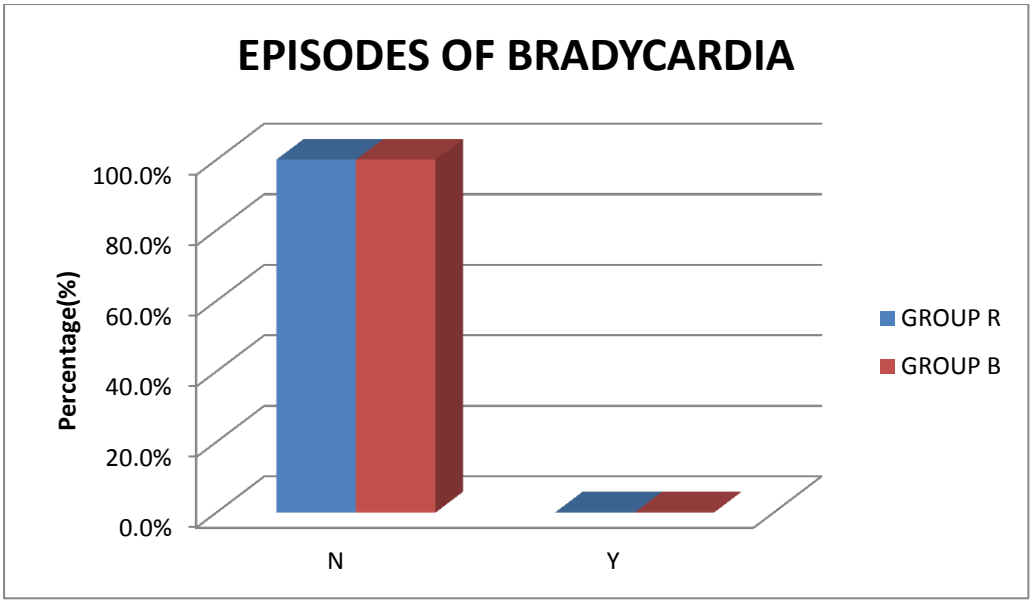
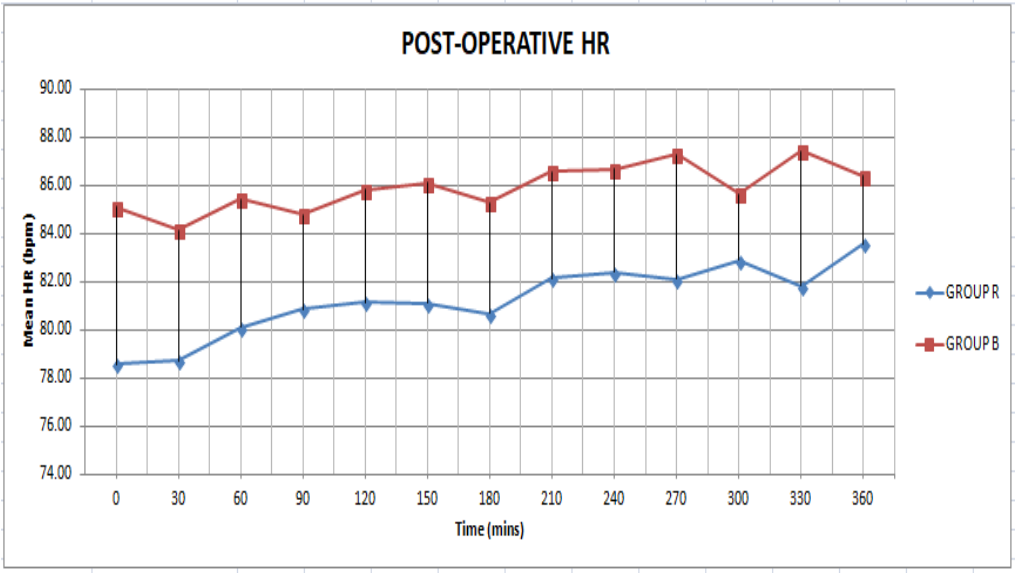


TABLE 16: COMPARISON OF STUDY GROUPS ACCORDING TO AMOUNT OF VASOPRESSOR NEEDED TO TREAT HYPOTENSION (mg)

	GROUP R		GROUP B		Z	p-value
	Mean	SD	Mean	SD		
Amount of vasopressor needed to treat hypotension (mg)	11.00	4.52	21.20	10.11	-2.176	0.030

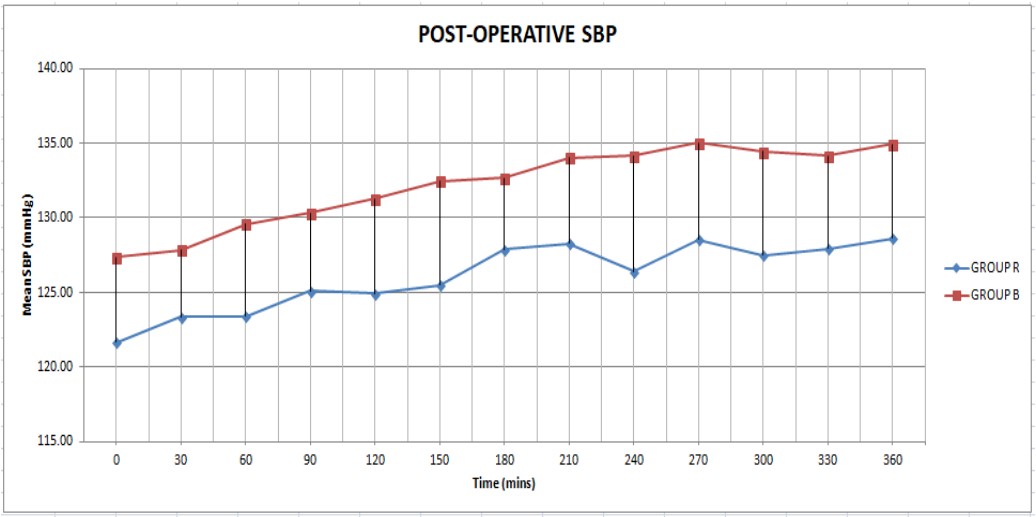
The amount of vasopressor (mg) needed to treat hypotension (defined as fall in SBP ≥ 20% from baseline) in group R (11.00 ± 4.52 mg) was significantly less than in group B (21.20 ± 10.11 mg) . The difference between both the study groups was statistically significant with p- value of 0.030. [Table 16]

FIGURE 22: TRENDS OF POST-OPERATIVE HR VALUES IN BOTH GROUPS



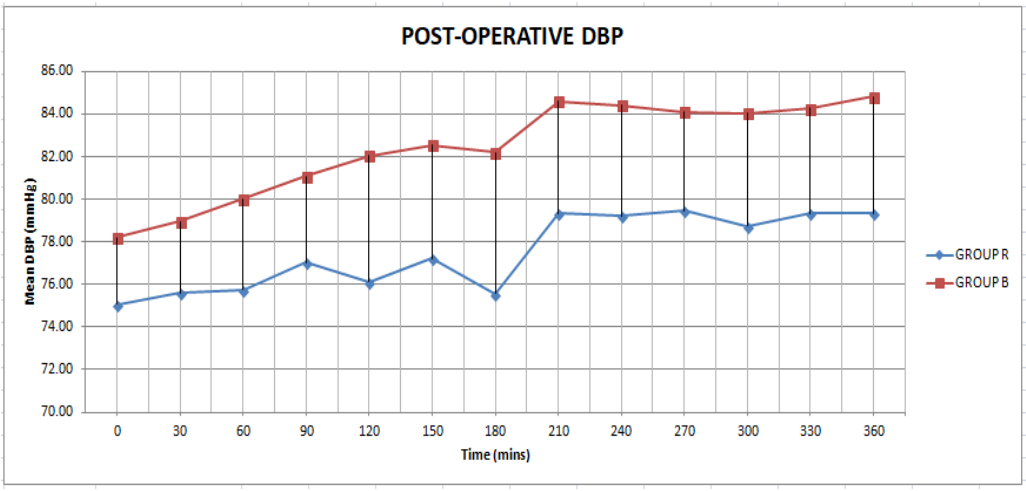
The HR was comparable in both the groups at all times (p>0.05). [Figure 22]

FIGURE 23: TRENDS OF POST-OPERATIVE SYSTOLIC BLOOD PRESSURE (SBP) VALUES IN BOTH THE GROUPS



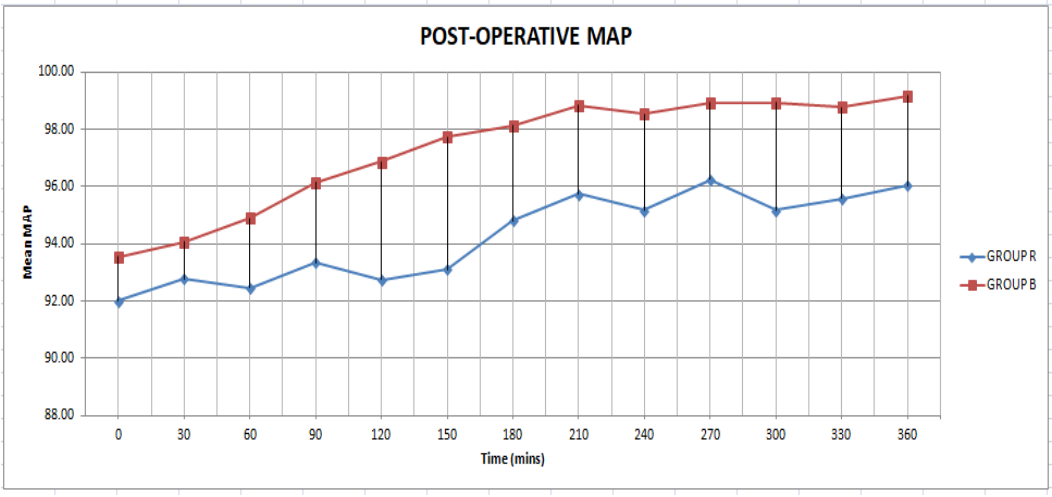
All the time points were statistically insignificant and comparable for Systolic blood pressure (SBP) between the two groups with p-value >0.05. [Figure23]

FIGURE 24: TRENDS OF POST-OPERATIVE DIASTOLIC BLOOD PRESSURE (DBP) VALUES IN BOTH THE GROUPS



All the time points were statistically insignificant and comparable for Diastolic blood pressure (DBP) between the two groups with p-value >0.05. [Figure24]

FIGURE 25: COMPARISON OF STUDY GROUPS ACCORDING TO POST-OPERATIVE MEAN ARTERIAL PRESSURE (MAP) VALUES



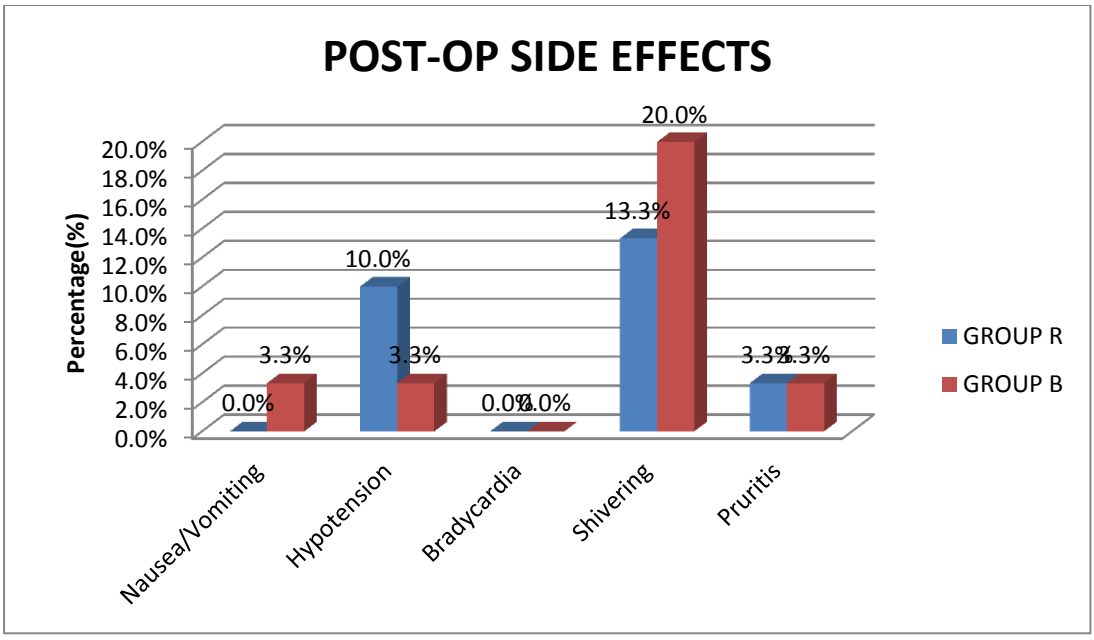
There was no statistically significant difference for the post-operative MAP values amongst the patients between the two groups (p>0.05). [Figure 25]

TABLE 17: COMPARISON OF STUDY GROUPS ACCORDING TO POST- OP SIDE EFFECTS

		GROUP R		GROUP B		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Nausea/Vomiting		30	100.0%	29	96.7%	59	1.017	0.313
	Y	0	0.0%	1	3.3%	1		
Hypotension		27	90.0%	29	96.7%	56	1.017	0.313
	Y	3	10.0%	1	3.3%	4		
Bradycardia		29	96.7%	30	100.0%	59	0	1.000
	Y	0	0%	0	0.0%	0		
Shivering		26	86.7%	24	80.0%	50	0.480	0.731
	Y	4	13.3%	6	20.0%	10		
Pruritis		29	96.7%	29	96.7%	58	0.000	1.000
	Y	1	3.3%	1	3.3%	2		

There was no statistically significant difference in post- op side effects amongst the patients between both the groups (p>0.05). [Table 17, figure 26]

FIGURE 26: COMPARISON OF STUDY GROUPS ACCORDING TO POST- OP SIDE EFFECTS



DISCUSSION

SAB is a preferred mode of anesthesia in patients posted for lower limb surgeries. Its ease of administration and maintenance of spontaneous respiration renders SAB better safety profile than general anesthesia in short duration as well as day care surgeries. This popularity of spinal anesthesia has resulted in continuous search for safer local anesthetics with better safety profile and reliable anesthesia. Since past two decades various combination of drugs have been studied and compared with respect to block characteristics and hemodynamic stabililty. This study compared two popular local anesthetics, 0.75% hyperbaric ropivacaine (recently launched hyperbaric formulation by NEON pharmaceuticals) with 0.5% hyperbaric bupivacaine using fentanyl as adjuvant in patients scheduled for lower limb surgeries. We compared these two drugs with respect to block characteristics i.e. two segment regression (duration of sensory block), onset of sensory and motor block, duration of motor block and need for first rescue analgesic (duration of analgesia). We also studied the episodes of hypotension and bradycardia to compare the hemodynamic parameters amongst both the study drugs.

According to a study by Kallio et al, on a milligram for milligram basis, the potency of ropivacaine relative to bupivacaine is two- thirds with regard to sensory block and half with regard to motor block.[8] Thus we chose 18.5 mg of ropivacaine and 12.5mg of bupivacaine as formulations of 0.75% hyperbaric ropivacaine and 0.5% hyperbaric bupivacaine along with 25 mcg of fentanyl to make a total drug dose of 3ml.

Sixty patients ASA I-III were enrolled in this double blind randomized controlled trial and statistically analyzed. All the patients in either of the two groups tolerated the study drug well and an adequate block needed to undergo lower limb surgeries was achieved in both the groups.

Two dermatome regression (Duration of sensory block)

The primary outcome of our study was to compare the two groups for duration of sensory block which was defined as period from intrathecal injection till two dermatome regression from the highest level of sensory block. It was observed that the patients in group R (99.27 ± 11.79 min) took significantly longer time for two dermatome regression than group B (85.17 ± 19.19 min) with P = 0.001. These findings are similar to the results by Shanmugam et al. in 2022 who observed that 0.75% hyperbaric ropivacaine (278 ± 5 min) showed significantly longer sensory block (defined as sensory regression to T10 level) in comparison to 0.5% hyperbaric bupivacaine (257 ± 9 min) with P <0.0001.[38] Similar results were observed by Chiari V et al in 2013 who compared equipotent doses of isobaric 0.75% ropivacaine (22.5 mg) and hyperbaric 0.5% bupivacaine (15 mg) and concluded that ropivacaine (117.2 ± 12.5 min) produced a significantly longer two dermatome sensory regression in comparison to bupivacaine (108.5 ± 10.61 min) with P<0.001, when used in SA.[39] However, our observations are in contrast with the two recent studies on intrathecal hyperbaric 0.75% ropivacaine. Kalbande et al in 2024 observed faster two segment regression with 3ml of hyperbaric 0.75% ropivacaine (91.12 ± 5.08 min) as compared to 3ml of hyperbaric 0.5% bupivacaine (100.65 ± 6.87 min) with P<0.001.[32] Similarly, Gupta et al in 2024 observed longer sensory blockade (defined as appearance of pain sensation at S2 dermatome) with 2.8 ml of hyperbaric 0.5% bupivacaine with 15 mcg of fentanyl when compared to equal dose of 0.75% hyperbaric ropivacaine with fentanyl but they didn't compare sensory block in terms of two segment regression.[36] These variations in sensory block findings can be due to difference in drug dosage, drug baricity, sample size or the type of surgery. It has also been observed in some studies that adding fentanyl to the intrathecal drug increases the sensory blockade without altering the motor blockade characteristics.[40]

Onset of sensory block

The onset of sensory block was described as time required till sensory blockade at T10 dermatome. The T10 dermatome level was chosen to define this parameter, as it was assumed that this level is required for initiation of lower limb surgeries. It was comparable between the two groups, group R (6.30 ± 3.66 min) and group B (7.0 ± 5.37 min) with P= 0.812. This could be explained by the fact that both these drugs have similar potency and pKa of 8.1.[19] Luck et al in 2008, they observed comparable results while comparing onset of sensory block amongst three groups- 0.5% hyperbaric bupivacaine (3ml), 0.5% hyperbaric levobupivacaine (3ml), and 0.5% hyperbaric ropivacaine (3ml). The onset as well as extent of sensory blockade depends mainly on two controllable factors i.e. baricity of study drug used and immediate position of the patient after administering the intrathecal drug.[23] In our study both these parameters were fixed and kept same in either of the two groups. Both groups were administered hyperbaric drugs and all patients were made to lie supine immediately after intrathecal drug administration. This could be the possible reason for comparable onset of sensory block in the two groups. Variable observations have been reported by different authors. Contrary to our study findings, Gupta et al observed a faster onset of sensory blockade in bupivacaine group where they used 2.8 ml of hyperbaric 0.5% bupivacaine with 15 mcg fentanyl in comparison to 0.75% hyperbaric ropivacaine 2.8 ml with 15 mcg fentanyl. It was 3.94 ± 0.76 min in bupivacaine group and 5.38 ± 0.62 min in ropivacaine group with P=0.001.[36] Another recent study comparing 0.75% hyperbaric ropivacaine (3ml) and hyperbaric 0.5% bupivacaine (3ml) defined onset of sensory block as appearance of tingling and numbness in patient after intrathecal injection. They found out that bupivacaine showed faster onset (92.46 ± 12.16 sec) in comparison to ropivacaine (153.90 ± 6.53 sec) in producing tingling sensation in patients(P<0.001).[32]

Gohil et al in 2023, compared 0.75% hyperbaric ropivacaine (3ml) and 0.5% hyperbaric bupivacaine (3ml) and concluded earlier sensory blockade. They defined onset of sensory block as loss to pinprick

sensation which was 2.6 ± 0.53 min in ropivacaine group and 3.0 ± 0.56 min in bupivacaine group with P= 0.006.[31]

It was observed that various studies have defined onset of sensory blockade in different ways which led to increased variability in results. Thus, addition of opioids, dose of study drug and definition of study parameter, all contribute to variation in study results.

Highest sensory level attained

The highest level of sensory block attained was T3 in both the groups. Out of 30 patients in ropivacaine group, 10 patients (33.3%) achieved T4 and 5 patients (16.7%) achieved T10 as the highest sensory block level. Likewise, 5 patients (16.7%) in bupivacaine group achieved T4 and 3 patients (10%) achieved T10 as the highest level of block. This parameter was comparable between the two groups p= 0.216. Similar results were found in other studies too.[12,28,32]

This might be attributed to the fact that the level of sensory block is influenced by five independent variables- drug dose, age, height, weight and gender of patient which were comparable in our study.[41]

Time required to achieve highest level of sensory block

In our study, the time required to achieve highest (maximum) level of sensory block was comparable between the two groups with p =0.337. These findings are in agreement with those of Gohil et al who compared 0.5% hyperbaric bupivacaine (3ml) with 0.75% hyperbaric ropivacaine (3ml). They also concluded that both these hyperbaric solutions took comparable time for highest cephalic spread. In their study, mean time taken for maximum cephalad spread was 7.96 ± 0.82 mins in ropivacaine group and 8.39 ± 1.24 mins in bupivacaine group with p >0.05.[31] The plausible reason for the same is, use of hyperbaric drugs in both the patients with similar volume.

Onset of motor block

We defined onset of motor blockade as time required to achieve MBS 3. It was found to be comparable in both the groups with p > 0.05. Garaniya et al compared 0.5% hyperbaric bupivacaine (3ml) with

0.75% hyperbaric ropivacaine (3ml) and observed that onset was 9.4 ± 2.1 mins in ropivacaine group and 8.2 ± 5.3 mins in bupivacaine group with p = 0.25.[30] These results are in congruence to our study findings. However, in a study by Gupta et al, 2.8 ml of hyperbaric 0.5% bupivacaine with 15 mcg fentanyl was compared with 0.75% hyperbaric ropivacaine 2.8 ml with 15 mcg fentanyl. They observed that bupivacaine group had faster onset of motor block (5.65 ± 0.82 mins) in comparison to ropivacaine group (7.51 ± 1.43 mins).[36] This could be because, ropivacaine is shown to be less lipophilic in comparison to bupivacaine (300:1000). It binds faster to Aδ and C fibers which are less myelinated small pain transmitting fibers. Bupivacaine binds readily to Aβ fibers which are large myelinated nerve fibers causing dense motor blockade.[19]

Duration of motor block

Duration of motor block was defined as time till motor regression to MBS 0. In ropivacaine group, motor regression occurred in 175.90 ± 40.81 mins while regression was relatively slower in bupivacaine group (205.07 ± 57.17 mins) with p = 0.052. Garaniya et al compared hyperbaric 0.5% bupivacaine (3ml) with 0.75% hyperbaric ropivacaine (3ml) and came to a conclusion that motor blockade with bupivacaine (160.5 ± 36.4 mins) is longer than with ropivacaine (124.3 ± 32.3 mins) with p = 0.0001.[30] Gohil et al compared 0.5% hyperbaric bupivacaine (3ml) and 0.75% hyperbaric ropivacaine (3ml) and observed that bupivacaine group showed motor blockade for 210 ± 13.19 mins in comparison to ropivacaine group (149.5 ± 8.64 mins).[31] This may be attributable to the fact that ropivacaine is less lipophilic. The lipid absorption of Ropivacaine : Bupivacaine is 300:1000. And since myelinated sheath of neurons is made up of lipids, absorption of ropivacaine is relatively very less in comparison to bupivacaine. Aδ and C fibers being small fibers, are responsible for pain sensations while Aβ fibers are large fibers responsible for motor action. And since ropivacaine has relatively more action on Aδ and C fibers, this causes better sensory - motor differentiation with ropivacaine resulting in faster

motor regression when compared to bupivacaine which produces a motor blockade that is dense and with a relatively slower regression.[19] This parameter is also helpful in patients admitted for daycare surgeries as it allows for early mobilization and recovery in ropivacaine group.

Duration of analgesia (first rescue analgesic)

In our study, we defined this parameter as time from intrathecal injection to demand for first rescue analgesic. We found that patients in bupivacaine group (300.73 ± 62.85 mins) had significantly longer duration of analgesia in comparison to ropivacaine group (264.33 ± 46.72 mins) with p= 0.013. Chatterjee at el also observed that time for first rescue analgesic with 3ml of hyperbaric 0.75% ropivacaine (190.8 ± 7.025 mins) was significantly earlier than with 3ml of 0.5% hyperbaric bupivacaine (253.7 ± 12.93 mins) with p <0.001.[29] Similar findings were observed by various other studies. [9,42] This could be because of early motor regression with ropivacaine which shows sensory motor differentiation causing earlier need for rescue analgesic. Contrary to this study, certain studies have shown comparable results between the two groups.[32,36]

Episodes of hypotension and bradycardia

Intraoperative hypotension was defined as fall in SBP ≥20% from baseline. In our study, 7 out of 30 patients (23.3%) in ropivacaine group experienced intraoperative hypotension which required ephedrine boluses while 16 patients (53.3%) in bupivacaine had hypotension requiring ephedrine boluses. Incidence of hypotension was found to be statistically significant between the two groups with p = 0.033. Amount of vasopressor required to treat hypotension in bupivacaine group (21.20 ± 10.11 mg) was significantly higher in contrast to ropivacaine group (11.00 ± 4.52 mg) with p = 0.030. Similar findings were observed by Whiteside et al who compared 0.5% hyperbaric bupivacaine in glucose 8% (3ml) with 0.5% hyperbaric ropivacaine in glucose 5% (3ml). They observed that 15% patients in

hyperbaric 0.5% ropivacaine group and 70% patients in hyperbaric 0.5% bupivacaine group experienced hypotension (defined as fall in SBP >30% from baseline) with p = 0.001.[37]

In a study done on fourty swines by Melo et al, to understand the effect of accidental intravascular injection of bupivacaine vs ropivacaine, either drug was injected at 4 ml/kg IV dose. They concluded that bupivacaine produced a more intense and prolonged suppression of cardiovascular system with significant reduction in cardiac index in comparison to ropivacaine group, which showed a transient reduction in cardiac index that returned to baseline within 10 minutes.[43] These effects of bupivacaine can be linked to the fact that bupivacaine binds to Na^{+}, K^{+}, Ca^{2+} channels present in the myocardium causing conduction blockade and development of arrhythmias in the patients.[44]

The cardiac effects have also been attributed to the structure of bupivacaine which is a R+ enantiomer. This enantiomer has shown to bind to both active and inactive Na^{+} channels in swine cardiac myocyte studies which caused intense hypotension and prolonged conduction blockade in them.[45]

LIMITATIONS OF OUR STUDY

1. Did not standardize the dose based on age, height, weight.
2. Performed study on elective cases.
3. Single center study

STRENGTHS OF OUR STUDY

1. Double blinded randomized controlled trial
2. Adequate sample size.
3. Our study sample included only one type of surgeries

SUMMARY AND CONCLUSION

This prospective study was conducted in the department of Anaesthesiology, Dayanand Medical College and Hospital, Ludhiana on sixty patients of ASA grade I-III of either gender scheduled for lower limb surgeries under SA. Patients were allocated to one of the two groups of 30 patients each according to computer generated random numbers. The technique of spinal anesthesia was standardized in both the groups. Group B was given 0.5% hyperbaric bupivacaine (3ml) - 2.5ml with 25mcg fentanyl intrathecally and Group R was administered 0.75% hyperbaric ropivacaine (3ml) 2.5ml with 25mcg fentanyl.

Block characteristics were observed as the following parameters –

Two segment sensory regression, onset and duration of sensory and motor blockade, need for first rescue analgesic and episodes of hypotension and bradycardia.

The following conclusions were drawn –

1. 0.75% hyperbaric ropivacaine showed longer two segment regression in comparison to bupivacaine when compared for the duration of sensory blockade.
2. The onset of sensory and motor blockade were comparable between the two groups.
3. Ropivacaine showed a faster regression of motor blockade in contrast to bupivacaine.
4. Need for first rescue analgesic was earlier in hyperbaric 0.75% ropivacaine group.
5. The episodes of hypotension were more in hyperbaric 0.5% bupivacaine group in contrast to the other group.

Thus, we concluded that intrathecal hyperbaric 0.75% ropivacaine provides satisfactory anaesthesia in comparison to bupivacaine with comparable onset, longer sensory blockade and faster motor regression while providing stable hemodynamics during the intraoperative period in patients scheduled for lower limb surgeries. With the availability of prepared solution of 0.75% hyperbaric

ropivacaine, it has become easier to administer this drug in patients undergoing short day care surgeries owing to its virtues of longer sensory blockade and faster regression of motor block. Ropivacaine shows the property of better sensory motor differentiation which causes motor block of shorter duration and thereby, promotes early ambulation and recovery after elective surgery.

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KEY TO MASTER CHART

Category	Code	Inference
Sex	M	Male
	F	Female
MBS		Modified Bromage Score
	0	Grade 0
	1	Grade 1
	2	Grade 2
	3	Grade 3
Hypotension and Bradycardia (Y/N)	Y	Yes
	N	No
Co-morbidities	CAD	Coronary Artery Disease
	CLD	Chronic Liver Disease
	CKD	Chronic Kidney Disease
	HCV+	Hepatitis C Virus positive
Type of Surgery	I and D	Incision and Drainage
	ORIF	Open Reduction Internal Fixation
	ACL	Anterior Cruciate Ligament
	F/U/C/O	Follow up case of
	BB	Both bone
	Exfix	External Fixator
	BKA	Below Knee Amputation
	TBW	Tension Band Wiring
	CRIF	Closed Reduction Internal Fixation
American Society of Anaesthesiologists	ASA I II III	Grade I II III

Vitals	HR	Heart rate
	MAP	Mean Arterial Pressure
	SBP	Systolic Blood Pressure
	DBP	Diastolic Blood Pressure
	SpO2	Oxygen saturation
VAS		Visual Analogue Score
SL		Sensory Level

S. no.	Patient Initials	Randomization No.	MRD No.	Age	Sex	Height (in cms)	Weight	BMI	ASA Grade	Comorbidities	Diagnosis	Surgery Performed	Date of Surgery	Time of administration of spinal anaesthesia	Time of start of surgery	Time of completion of surgery	Duration of Surgery	Time of patient received in PACU
1	SS	1	1392409	23	M	175.26	65	21.2	I	None	Left Medial Meniscus Tear	Arthroscopic Meniscal Repair	10-07-2022	12:55 PM	1:10 PM	2:00 PM	50 mins	2:15 PM
2	AY	2	1346648	20	F	167.64	65	23.1	I	None	Bony Deformity Right knee	Right knee supracondylar osteotomy	10-08-2022	1:30 PM	2:00 PM	4:20 PM	140 mins	4:30 PM
3	RK	3	1377991	64	M	167.64	63	22.4	III	Hypertension, Diabetes Type 2	Foot Crush Injury	Left foot skin grafting	10-10-2022	1:50 PM	2:10 PM	3:20 PM	70 mins	3:30 PM
4	HS	4	1395933	56	M	165.1	75	27.5	I	None	Right Tibial + Fibular fracture	Debridement and Exfix	10-12-2022	10:10 AM	10:30 AM	12:40 PM	130 mins	12:45 PM
5	GS	5	1046678	27	M	177.8	60	19	I	None	Ilizarov In situ	Ilizarov Removal	26/10/2022	11:20 AM	11:30 AM	12:30 AM	60 mins	12:40 PM
6	HS	6	1395933	56	M	170.18	9	31.1	II	Obese class 1	Right leg wound	Split Skin Grafting	28/10/2022	10:50 AM	11:00 AM	12:15 PM	75 mins	12:25 PM
7	SK	7	301755	45	M	165.1	75	27.5	I	None	Wound on left leg	Split Skin Grafting	29/10/2022	1:40 PM	1:55 PM	2:25 PM	30 mins	2:35 PM
8	SS	8	1429555	35	M	177.8	75	23.7	I	None	Right Femoral Abscess	I and D	30/10/2022	1:45 PM	2:35 PM			
9	MS	8	1430876	37	M	172.72	88	29.5	II	None	Right ACL Tear	Right ACL Repair	14/12/2022	1:35 PM	2:15 PM	3:30 PM	75 mins	3:50 PM
10	HR	9	1428540	56	M	165.1	63	23.1	III	Hypertension	Left Tibial Fracture	Left Tibial Nailing	14/12/2022	10:25 AM				
11	AK	9	1421091	58	F	160.02	50	19.5	I	None	Left Tibial Fracture	Left Tibial Plating + Grafting	14/12/2022	9:45 AM	10:10 AM	12:25 PM	135 mins	12:47 PM
12	PK	10	1429801	53	M	165.1	80	29.3	I	None	Left Femur Fracture	Left Femur Nailing	16/12/2022	1:10 PM	1:20 PM	2:40 PM	70 mins	2:45 PM
13	KR	11	1325296	64	F	154.94	70	29.2	III	Hypertension, Diabetes Type 2	Trimalleolar Implant	Implant Removal	16/12/2022	1:15 PM	1:30 PM	2:05 PM	35 mins	2:15 PM
14	RA	12	1432562	25	M	160.02	70	27.3	I	None	Midshaft femur fracture	CRIF Right Femur	16/12/2022	1:30 PM	1:40 PM	2:15 PM	35 mins	2:20 PM
15	IK	13	1368414	17	M	152.4	55	23.7	I	None	Right Infected Tibial Implant	Implant removal and skin grafting	16/12/2022	5:00 PM	5:10 PM	7:20 PM	130 mins	7:35 PM
16	RK	14	1433684	52	M	172.72	85	28.5	I	None	Left Tibial Fracture	Exfix application left knee	17/12/2022	7:00 PM	7:10 PM	7:30 PM	20 mins	7:40 PM
17	AP	15	1419866	43	M	175.26	102	33.2	I	None	Infected leg wound	Wound wash and suturing	17/12/2022	3:25 PM	3:40 PM	4:45 PM	65 mins	5:00 PM
18	DB	16	1435608	42	M	177.8	92	29.1	I	None	Left thigh gunshot wound	Left thigh wound debridement	22/12/2022	2:20 PM	2:45 PM	3:10 PM	25 mins	3:30 PM
19	AS	17	1437802	22	M	175.26	53	17.3	I	None	Left leg wound	Debridement and Exfix	27/12/2022	4:15 PM	4:30 PM	5:45 PM	75 mins	6:15 PM
20	BS	18	1251486	38	M	172.72	85	28.5	I	None	Discharging Sinus	Sequestrectomy	29/12/2022	1:30 PM	2:25 PM	2:40 PM	15 min	3:00 PM
21	AS	19	1445894	39	M	172.72	75	25.1	I	None	Fracture Right Calcaneum	ORIF Calcaneum	29/12/2022	12:15 PM	1:45 PM	2:45 PM	60 mins	3:00 PM
22	CS	20	1432717	21	M	167.64	60	21.3	I	None	Left Knee pain	Left Diagnostic Arthroscopy	29/12/2022	11:45 PM	12:25 PM	12:40 PM	15 mins	1:00 PM
23	AM	21	1439853	23	M	165.1	85	31.2	I	None	Left Patellar fracture	TBW left patella	31/12/2022	2:10 PM	2:30 PM	3:55 PM	85 mins	4:10 PM
24	PK	22	1435992	52	M	162.56	64	24.2	II	Diabetes Type 2	Infected Right Knee	Arthroscopic Knee Lavage	30/12/2022	1:55 PM	2:10 PM	3:10 PM	60 mins	3:20 PM
25	MK	23	1446020	18	M	180.34	80	24.6	I	None	Right Ankle wound	Debridement	16/1/2023	2:45 PM	2:55 PM	3:35 PM	40 mins	3:45 PM
26	SS	24	1445990	62	M	172.72	65	21.8	III	CAD, Hypertension	Fracture Distal femur and Tibia	ORIF Distal Femur and Exfix	17/1/2023	10:00 PM	10:30 PM	1:00 PM	150 mins	1:00 PM
27	HS	25	1431193	60	M	167.64	75	26.7	III	Hypertension, Diabetes Type 2, CKD	Ifected stump	Debridement and wound wash	17/1/2023	1:45 PM	2:00 PM	3:00 PM	60 mins	3:10 PM
28	JS	26	1367451	22	M	180.34	70	21.5	I	None	Patellar implant in situ	Implant Removal	25/1/2023	7:35 PM	7:45 PM	8:05 PM	20 mins	8:15 PM
29	PK	27	1429168	52	M	167.64	55	19.6	III	Uncontrolled Hypertension	Right Septic Knee	Right Knee Arthotomy	18/1/2023	10:20 AM	10:35 PM	12:50 PM	135 mins	1:00 PM
30	VS	28	1448487	41	M	182.88	90	26.1	II	Overweight	Fracture left tibia	Exfix Left Leg	20/1/2023	10:15 AM	10:40 AM	11:00 AM	20 mins	11:05 AM
31	AK	29	1453645	21	M	170.18	55	19	I	None	Frature patella and fibular head	Left Fibular plating and TBW	30/1/2023	7:40 PM	8:00 PM	9:50 PM	110 mins	10:10 PM
32	GS	30	1414549	36	M	172.72	80	26.8	II	Diabetes Type 2	Right leg stump growth	Stump Closure	02-03-2023	2:15 PM	2:40 PM	4:00 PM	80 mins	4:05 PM
33	RG	31	1457222	51	F	165.1	63	23.1	II	Hypertension	Frature Tibia	Tibia Nailing	02-05-2023	10:00 AM	10:30 AM	12:00 PM	90 mins	12:00 PM
34	SK	32	1464058	25	M	180.34	95	29.2	II	None	Frature BB leg	BB leg plating	03-01-2023	1:40 PM	2:10 PM	4:30 PM	140 mins	4:40 PM
35	BK	33	1472375	48	F	160.02	63	24.6	I	None	F/U/C/O Tibial Implant	Implant removal left tibia	03-01-2023	7:20 PM	7:40 PM	8:30 PM	50 mins	8:35 PM
36	SK	34	1336883	52	M	187.96	100	28.3	I	None	Spur Right sole	Spur excision	03-06-2023	10:05 AM	10:30 AM	11:10 AM	40 mins	11:20 AM
37	R	35	1479220	40	F	157.48	68	27.4	I	None	Left Tibial Fracture	Left Tibial Plating	16/3/2023	1:30 PM				
38	RM	35	1495306	48	M	165.1	72	26.4	II	Hypertension	Ankle Fracture	Ankle Exfix	04-07-2023	9:00 PM	9:15 PM	10:30 PM	75 mins	10:35 PM
39	DS	36	1498894	46	M	170.18	80	27.6	III	CLD, Diabetes Mellitus Type 2	Implant Abscess Left Knee	I and D left Knee	17/4/2023	12:30 PM	12:45 PM	1:45 PM	60 mins	1:50 PM
40	JS	37	1476108	24	M	180.34	86	26.4	II	None	Wound on Right leg	Debridement Right Leg	18/4/2023	6:15 PM	6:35 PM	7:15 PM	40 mins	7:20 PM
41	HS	38	1500230	18	M	190.5	85	23.4	I	None	Post Traumatic Quadriceps Injury	Quadriceps tendon release	20/4/2023	2:00 PM	2:40 PM	4:00 PM	80 mins	4:05 PM
42	AK	39	1433792	23	M	170.18	66	22.8	II	None	F/U/C/O Exfix Removal	Exfix Removal	24/4/2023	12:40 PM	12:50 PM	1:30 PM	40 mins	1:35 PM
43	CA	40	1479837	25	M	182.88	95	28.4	I	None	Left Tibial Implant	Tibial Implant Removal	27/4/2023	12:00 PM	12:30 PM	1:40 PM	70 mins	1:45 PM
44	BS	41	164084	51	M	177.8	85	26.9	I	None	Osteoma Tibia	High Tibial Osteotomy	28/4/2023	11:50 PM	12:50 PM	2:00 PM	70 mins	2:05 PM
45	MS	42	1249344	57	M	165.1	72	26.4	II	Diabetes Type 2	Tibial Fracture	Tibial Plating	30/4/2023	2:00 PM	2:15 PM	3:30 PM	75 mins	3:30 PM
46	KS	43	1460924	45	M	182.88	75	22.4	III	CKD, Hypertension	Fracture BB Leg	BB leg plating	05-07-2023	1:20 PM	1:40 PM	3:20 PM	100 mins	3:30 PM
47	DS	44	1497619	56	M	152.4	60	25.8	II	None	Infected wound right leg	I and D	14/6/2023	10:08 AM	10:30 AM	11:20 AM	50 mins	11:30 AM
48	RS	45	1506352	50	M	165.1	70	25.7	II	Hypertension, Diabetes Type 2	F/U/C/O Exfix Right Leg	Skin Grafting	14/6/2023	1:15 PM	1:25 PM	2:10 PM	45 mins	2:30 PM
49	A	46	1011449	20	M	177.8	78	24.7	I	None	F/U/C/O Tibial Implant	Implant Removal	14/6/2023	11:24 AM	11:54 AM	12:45 PM	51 mins	1:00 PM
50	AS	47	1443923	30	M	157.48	70	30.1	II	HCV +	Infected amputated limb	Revision Amputation	16/6/2023	7:52 PM	8:05 PM	9:00 PM	55 mins	9:00 PM
51	RK	48	1315750	42	F	162.56	76	28.8	III	Diabetes Type 2	Varicose Veins	Varicose Vein Ligation	16/6/2023	6:20 PM	6:40 PM	8:40 PM	120 mins	8:45 PM
52	SS	49	1467708	36	M	167.64	96	35.9	II	None	Right Leg Tibial Exfix	Sequestrectomy	18/6/2023	1:26 PM	1:40 PM	3:15 PM	95 mins	3:20 PM
53	LS	50	1538778	27	M	180.34	90	27.7	I	None	Gangrenous leg	BKA	22/6/2023					
54	SS	50	968167	38	M	167.64	77	27.4	I	None	Meniscal Tear	Arthroscopy	23/6/2023	12:05 PM	1:00 PM	1:30 PM	30 mins	1:40 PM
55	TS	51	1491102	30	M	165.1	68	24.9	III	HCV +	Tibial Wound	Debridement	23/6/2023	9:45 PM	9:50 PM	10:15 PM	25 mins	10:20 PM
56	SS	52	1505503	49	M	172.72	80	26.8	II	None	Infected Femur Plating	Femur Nailing	23/6/2023	12:44 PM	1:00 PM	2:10 PM	70 mins	2:15 PM
57	AS	53	1557463	29	M	180.34	94	28.9	II	None	Fracture Tibia	ORIF Tibia	28/7/2023	7:20 PM	7:30 PM	9:15 PM	105 mins	9:20 PM
58	SS	54	1560214	28	M	165.1	65	23.8	II	None	Fracture Tibia	Tibia Nailing	28/7/2023	2:00 PM	2:45 PM	4:00 PM	75 mins	4:00 PM
59	AS	55	1584654	60	M	162.56	65	24.6	II	Hypertension	Frature Tibia	Tibia Plating	29/7/2023	1:00 PM	1:30 PM	3:30 PM	120 mins	3:45 PM
60	BS	56	1561247	47	M	172.72	80	26.8	I	None	Halgund Deformity	Bone Excision	08-01-2023	11:00 AM	11:15 AM	11:55 AM	40 mins	12:00 PM
61	SK	57	1594063	60	F	152.4	62	26.7	II	None	Right Knee Injury	Meninsectomy Right knee	21/9/2023	11:10 AM	11:45 AM	12:25 PM	40 mins	12:40 PM
62	VK	58	1561410	44	M	170.18	90	31.1	II	Obese class 1	Tibial bone growth	Bone Excision and Grafting	22/9/2023	12:00 PM	12:15 PM	1:40 PM	85 mins	1:45 PM
63	MP	59	902525	65	M	162.56	64	24.2	II	None	Fracture Tibia	Tibial Exfix	22/9/2023	9:25 PM	9:40 PM	10:15 PM	35 mins	10:30 PM
64	GS	60	1595638	42	M	175.26	94	30.6	I	None	Osteomyelitis Distal Femur	I and D	23/9/2023	8:50 PM	9:10 PM	9:50 PM	40 mins	10:05 PM

S. no.	Total duration of motor block	Time of rescue analgesic administration	HR_Baseline	HR_0	HR_2	HR_4	HR_6	HR_8	HR_10	HR_15	HR_30	HR_45	HR_60	HR_75	HR_90	HR_105	HR_120	HR_150	HR_180	SBP_Baseline	SBP_0	SBP_2	SBP_4	SBP_6	SBP_8	SBP_10	SBP_15	SBP_30	SBP_45	SBP_60	SBP_75	SBP_90	SBP_105
1	145 mins	300 mins	69	70	72	76	73	73	71	63	69	60	64	68						130	146	123	130	124	132	132	124	130	130	124	122		
2	240 mins	270 mins	76	84	82	90	94	90	92	71	74	79	72	72	73	90	104	110	112	120	130	133	128	74	106	90	119	114	142	109	110	121	116
3	100 mins	310 mins	96	98	92	98	96	94	96	92	85	74	80	82						136	130	134	138	129	130	140	151	138	138	140	142	144	
4	185 mins	315 mins	100	100	101	104	100	96	92	88	84	80	82	83	76	79	82	85		120	118	114	104	87	98	92	99	92	82	99	96	96	100
5	140 mins	210 mins	80	82	78	70	66	63	67	63	63	58	64	62						120	120	110	102	102	109	104	100	98	100	100	99		
6	185 mins	185 mins	98	100	102	103	107	102	95	95	87	90	87	83	83					136	138	130	100	110	110	120	117	100	102	108	115	113	
7	85 mins	145 mins	78	81	90	94	90	82	82	92	75	78								140	140	131	136	134	131	131	131	127	130				
8																																	
9	120 mins	255 mins	60	64	65	68	68	70	66	67	55	53	52	51	53	55	60			133	140	154	150	146	140	141	124	129	129	136	134	133	143
10																																	
11	180 mins	272 mins	85	86	93	96	92	92	92	92	86	82	83	75	78	80	89	86	88	131	137	125	118	123	124	117	124	129	113	11	109	100	106
12	185 mins	275 mins	99	96	96	100	101	104	106	99	103	101	102	103	108					126	126	128	130	130	132	138	101	109	110	116	117	124	
13	210 mins	300 mins	76	82	90	96	104	82	79	68	65	71								190	199	195	180	180	160	100	150	150	146				
14	130 mins	310 mins	105	115	121	126	111	112	110	111	100	107	91	90	95					130	130	110	98	111	90	88	93	105	96	85	100	96	
15	150 mins	185 mins	86	86	80	78	71	71	76	73	85	67	72	85	97	96	80	87		129	131	132	130	138	110	121	125	134	121	126	118	137	121
16	160 mins	280 mins	76	95	80	82	77	81	75	76	82									141	153	150	152	149	152	146	152	138					
17	305 mins	395 mins	90	102	100	102	100	106	94	88	81	72	71	70						163	152	146	140	132	126	113	103	1055	127	121	121		
18	190 mins	310 mins	103	102	104	98	87	77	77	94	90	98	98							120	124	114	108	90	82	88	108	92	102	101			
19	195 mins	300 mins	120	120	113	119	108	110	120	122	123	126	130	132	136	126	124			134	130	132	146	129	131	129	131	120	114	112	100	121	121
20	240 mins	360 mins	100	98	99	99	97	95	95	88	91	85	87	86						150	159	154	153	126	115	115	107	120	127	128	124		
21	165 mins	375 mins	99	98	96	94	96	94	98	88	80	74	80	84	83	94	94	95		131	130	125	128	133	126	129	118	126	103	94	92	113	107
22	90 mins	275 mins	112	110	118	110	119	124	108	100	100	100	112							120	120	120	118	96	102	110	102	100	100	100			
23	210 mins	300 mins	106	108	99	98	98	90	83	80	75	70	72	89	87	98				145	144	143	140	138	127	110	118	112	110	108	114	116	116
24	235 mins	295 mins	66	76	74	72	68	68	66	67	63	61	66							126	120	114	110	114	113	115	115	115	113	112			
25	150 mins	180 mins	107	108	108	110	110	108	105	104	102	102								138	148	148	142	146	148	142	144	148	144				
26	180 mins	240 mins	78	86	82	86	89	88	89	89	80	71	73	62	63	64	66	74		120	116	120	116	88	116	103	89	88	100	100	110	114	118
27	175 mins	235 mins	109	97	95	93	100	103	99	97	98	102	104	103						154	165	160	159	160	162	167	164	152	148	140	151		
28	200 mins	320 mins	88	89	87	88	80	73	71	65	68									118	116	116	110	112	110	105	105	104					
29	210 mins	210 mins	86	90	95	94	91	90	90	91	86	82	84	81	82	84	86	89		100	100	100	95	96	95	100	104	100	100	100	100	102	104
30	75 mins	170 mins	125	112	95	90	95	87	95	87	88	87	84	86						145	140	154	159	159	153	162	161	153	141	150	146		
31	240 mins	210 mins	89	80	75	76	68	69	71	62	63	54	53	56	58	54	56	58	57	130	130	132	132	133	136	130	128	126	120	120	124	122	124
32	230 mins	230 mins	100	102	112	120	122	130	130	120	113	106	107	108	110	112	114			142	140	129	135	136	120	112	113	110	110	110	110	114	110
33	120 mins	180 mins	80	86	84	82	78	76	74	72	81	70	70	65	76	83				127	130	124	120	118	120	117	117	122	110	111	113	108	110
34	180 mins	240 mins	82	80	78	80	80	79	75	79	85	74	72	79	78	80	88	82	84	146	148	142	147	146	147	131	135	135	126	126	127	128	128
35	135 mins	315 mins	110	99	100	98	92	94	99	90	83	84	84	86						124	126	122	120	118	120	126	111	107	120	124	124		
36	165 mins	255 mins	64	80	82	88	86	86	84	85	76	81	77	80						140	142	137	130	128	123	120	123	125	114	110	120		
37			66	62	65	62	60	61	62	64										108	108	110	107	108	106	108	110					
38	215 mins	335 mins	100	102	100	97	98	97	107	107	104	98	102	104	107					128	130	102	80	70	101	107	97	104	102	104	108	110	
39	200 mins	320 mins	78	70	71	69	78	68	69	71	66	66	71	70						161	161	162	161	158	154	140	147	149	145	133	140		
40	125 mins	245 mins	70	69	72	70	76	78	88	79	70	70	69							126	124	118	124	121	126	126	129	116	122	120			
41	155 mins	245 mins	76	72	70	72	73	74	70	68	70	72	68	70	72	65	67			150	148	150	146	142	140	142	146	146	138	142	140	136	138
42	235 mins	360 mins	102	100	98	110	108	102	96	100	100	98								134	130	127	127	117	120	122	126	119	120				
43	195 mins	345 mins	72	76	78	70	82	73	72	71	64	65	58	65	61	62				130	130	124	125	129	120	116	119	119	114	121	129	128	130
44	165 mins	255 mins	74	77	77	78	79	76	84	76	76	71	70	65	60	62	64	65		174	174	171	170	161	156	156	156	148	145	154	162	162	164
45	210 mins	300 mins	61	62	64	66	62	68	67	61	60	58	60	62	64					160	158	156	150	136	130	120	106	132	136	108	134	116	
46	160 mins	280 mins	100	100	99	98	93	94	93	90	84	95	84	86	89	88	88			170	172	180	150	145	144	142	152	140	151	103	126	116	140
47	262 mins	382 mins	77	70	84	76	87	91	92	86	78	68	71	97	90					129	125	121	114	114	105	112	103	92	122	120	110	110	
48	255 mins	315 mins	127	120	127	128	127	129	130	135	123	104	104							158	146	138	130	123	120	92	126	131	145	142			
49	174 mins	270 mins	86	86	79	80	80	81	73	76	66	70	82	77	64	79				126	126	130	137	137	134	128	124	127	121	126	132	131	133
50	218 mins	278 mins	109	95	92	90	89	85	85	83	82	80	76							118	113	118	117	119	114	112	111	108	110	112			
51	235 mins	295 mins	100	100	99	104	97	87	80	81	85	74	68	74	68	69	76			138	140	134	134	138	112	115	117	115	122	121	133	128	124
52	320 mins	420 mins	70	73	79	71	77	70	58	57	59	60	61	64	60	59				125	121	107	116	108	106	103	101	110	108	106	108	110	112
53			100	103	94	95	97	94	95											130	134	138	139	125	126	128						
54	125 mins	275 mins	90	84	89	87	90	80	83	80	73	80	70	71	72					120	120	123	123	118	116	113	112	110	108	103	110	114	
55	185 mins	305 mins	110	112	112	119	126	114	109	110	86									130	136	136	136	136	131	122	115	109					
56	270 mins	360 mins	90	94	89	84	83	83	81	80	74	70	68	67	68					150	153	136	138	135	134	130	121	132	130	132	139	136	
57	210 mins	270 mins	92	116	110	94	68	78	82	90	94	88	78	77	87	75	76	87		128	112	110	96	96	98	120	122	117	115	118	121	121	122
58	270 mins	330 mins	112	116	110	112	116	112	113	110	82	77	73	84	103	76	82			130	136	134	130	128	124	120	116	119	116	121	116	123	129
59	255 mins	315 mins	100	100	99	104	97	86	82	84	86	85	76	78	74	68	69	76		138	140	134	134	138	112	114	118	116	124	122	134	128	126
60	180 mins	300 mins	82	74	69	68	70	72	66	64	68	71	70							136	118	99	98	104	108	111	109	110	110	105			
61	210 mins	240 mins	83	76	75	75	73	73	74	74	72	70	65	67						156	156	136	133	134	141	141	136	137	133	137	138		
62	285 mins	345 mins	90	100	108	120	110	108	106	104	90	86	88	92	90	86				130	136	120	114	110	104	104	90	110	116	124	124	120	122
63	215 mins	305 mins	70	72	60	70	70	69	68	73	60	60	62							130	130	132	128	125	101	109	116	123	110	105			
64	225 mins	255 mins	67	64	61	62	63	64	62	66	60	60	61	69						151	147	140	137	140	139	139	135	122	132	141	131		

S. no.	SBP_120	SBP_150	SBP_180	DBP_Baseline	DBP_0	DBP_2	DBP_4	DBP_6	DBP_8	DBP_10	DBP_15	DBP_30	DBP_45	DBP_60	DBP_75	DBP_90	DBP_105	DBP_120	DBP_150	DBP_180	MAP_Baseline	MAP_0	MAP_2	MAP_4	MAP_6	MAP_8	MAP_10	MAP_15	MAP_30	MAP_45	MAP_60
1				78	60	55	55	65	65	56	58	65	63	61	63						85	99	83	82	87	92	93	87	89	90	89
2	112	116	126	83	80	75	80	50	80	60	47	59	63	57	60	55	60	69	70	78	98	104	101	98	57	90	68	96	75	75	79
3				86	80	84	82	79	80	80	82	74	77	80	82	82					100	110	108	106	108	110	108	113	104	109	108
4	107	129		83	70	66	56	51	54	53	62	59	54	58	64	65	64	70	75		86	83	80	74	64	68	67	74	69	64	72
5				70	70	64	64	64	68	62	58	56	60	50	60						87	86	82	89	89	84	78	77	74	74	76
6				90	89	79	75	65	65	75	68	68	67	69	70	77					110	106	92	84	81	81	90	86	81	81	82
7				95	106	91	84	86	82	89	102	91	90								111	123	107	106	102	104	100	115	106	110	
8																															
9	147			70	70	74	68	68	62	76	65	68	48	63	64	59	63	65			98	105	113	110	100	96	105	100	98	99	101
10																															
11	114	116	124	88	65	70	65	68	69	79	77	77	71	66	64	60	62	68	70	80	109	97	95	86	99	100	95	95	98	88	83
12				86	86	88	90	89	87	82	66	68	70	69	70	80					99	99	98	99	98	98	100	80	80	80	76
13				98	100	102	100	95	80	60	80	81	79								138	140	131	120	124	110	72	103	104	102	
14				80	78	65	58	49	50	33	43	45	41	32	50	50					106	105	80	72	69	60	54	59	69	64	60
15	126	130		80	81	72	70	71	69	71	75	72	76	84	78	83	83	84	70		96	107	102	94	104	87	95	93	96	96	106
16				96	101	100	102	95	94	90	94	94									117	122	116	117	115	19	119	113	110		
17				113	96	88	82	76	68	64	60	60	75	73	82						131	126	119	118	110	100	86	78	78	99	95
18				85	62	54	54	35	38	39	59	42	45	48							96	74	69	68	56	58	60	74	59	66	69
19	121			94	91	90	83	84	82	88	81	70	68	70	65	78	80	86			105	105	102	98	100	100	101	97	90	88	89
20				84	88	86	85	78	72	70	66	74	78	85	83						118	120	116	116	91	87	86	84	91	91	99
21	108	109		85	82	80	86	85	81	84	75	54	58	55	59	62	68	67	67		101	100	98	100	98	96	97	90	65	75	68
22				70	68	62	60	57	54	65	56	51	56	56							92	90	82	80	72	73	79	70	69	71	68
23				86	64	65	63	63	55	54	61	62	60	62	63	63	67				114	104	100	98	96	87	78	85	84	79	80
24				78	70	74	65	69	67	69	67	68	66	64							97	95	93	80	86	84	88	87	88	84	80
25				90	90	92	90	92	94	90	92	94	92								90	95	108	107	106	108	100	102	108	106	
26	130	119		64	65	64	69	58	69	66	56	57	59	62	65	67	72	72	76		88	84	88	84	66	83	80	67	67	72	75
27				98	103	102	99	99	99	102	99	96	99	97	104						122	132	130	130	130	121	133	127	120	118	112
28				82	80	81	72	74	72	68	68	66									97	95	96	90	92	92	81	81	81		
29	100	100		74	70	60	47	48	65	68	69	72	70	68	64	72	74	68	70		88	75	74	68	70	78	80	83	83	82	81
30				103	100	102	104	100	90	101	96	91	94	98	94						119	108	112	114	118	116	126	119	117	113	120
31	126	124	120	80	80	82	82	65	75	80	76	74	67	68	74	72	74	76	74	70	102	95	94	94	93	92	94	92	90	87	88
32	112			92	89	72	77	78	70	63	63	58	70	68	70	74	72	70			112	110	101	97	97	87	82	80	78	82	80
33				86	89	84	82	79	80	80	80	72	74	73	75	74	70				98	99	98	97	94	96	94	96	95	92	89
34	149	136	140	80	86	81	85	80	79	82	85	77	76	71	71	75	74	86	82	84	109	107	104	107	109	111	107	104	101	99	94
35				82	84	82	80	78	78	73	70	80	62	65	70						94	92	89	89	90	92	94	89	89	90	93
36				79	82	95	90	89	84	81	78	85	74	74	80						102	104	108	104	101	100	99	90	100	87	86
37				76	77	82	70	72	74	72	82										89	89	90	87	88	88	88	90			
38				80	80	68	40	30	61	62	54	67	60	62	64	66					96	97	79	53	43	78	81	68	79	75	76
39				110	110	108	102	98	98	96	101	91	93	86	89						124	124	126	124	120	118	116	124	117	118	107
40				80	80	71	73	71	69	69	67	70	65	68							95	95	87	90	88	88	88	88	85	84	85
41	136			92	90	92	90	88	82	86	89	89	79	80	82	80	82	82			111	109	111	109	106	104	106	112	108	102	106
42				90	90	84	82	76	72	70	77	77	72								102	99	97	96	89	90	92	95	94	92	
43				78	74	74	72	71	56	65	63	68	68	66	71	72	74				92	90	89	90	86	80	82	83	84	83	88
44	160	160		114	112	117	11	110	107	103	105	110	98	97	101	106	104	102	100		144	139	134	132	132	125	123	126	117	114	118
45				90	86	82	80	78	68	60	58	68	68	52	68	66					113	110	107	103	97	889	80	74	89	91	71
46	137			90	102	92	90	85	86	88	87	73	83	70	77	70	79	74			132	132	125	109	110	110	110	112	101	111	81
47				82	88	71	71	71	65	71	64	58	64	66	68	70					99	105	92	89	89	83	90	80	72	93	93
48				98	92	82	80	79	74	61	81	86	99	93							109	108	102	99	98	98	72	94	103	113	110
49				72	74	61	74	72	63	65	77	60	71	61	65	60	70				88	89	91	95	94	87	87	92	89	88	87
50				71	93	72	71	76	66	68	63	70	72	70							90	88	92	90	94	85	89	86	84	85	84
51	123			82	86	80	82	82	66	72	68	69	78	79	72	73	72	79			104	106	102	102	104	87	91	89	90	98	100
52				83	90	76	68	61	60	59	62	57	60	60	62	70	72				100	104	86	82	82	80	74	76	80	82	80
53				94	95	90	78	62	72	74											106	108	100	98	88	96	96				
54				71	70	74	74	74	72	75	70	71	68	64	68	77					91	90	91	91	86	84	89	84	86	82	80
55				80	82	86	67	79	67	64	57	54									97	100	103	90	98	88	83	77	72		
56				100	98	93	94	89	87	82	68	88	84	84	88	86					124	116	112	109	108	107	102	90	106	103	101
57	118	127		76	70	70	47	50	50	65	67	68	69	70	68	71	72	74	81		94	88	86	68	72	74	84	88	86	87	90
58	121			86	89	86	82	80	76	70	72	75	72	76	79	88	86	80			101	103	102	98	96	92	87	87	90	81	94
59	124	126		82	86	80	82	82	66	73	66	70	78	78	72	72	74	72	74		104	106	102	102	104	87	91	87	89	98	96
60				81	74	66	62	68	71	74	72	72	73	72							99	88	77	74	80	83	86	85	85	87	83
61				89	82	66	66	66	66	66	70	67	68	70	68						117	112	98	93	93	98	98	98	97	96	98
62				90	94	80	72	70	68	70	40	70	72	76	72	72	70				103	108	93	86	83	80	81	57	83	87	92
63				84	80	78	76	72	68	65	66	64	66	57							88	88	88	86	84	81	79	77	87	79	74
64				85	70	68	60	65	72	72	77	57	66	69	65						105	90	95	96	98	90	90	95	100	92	101

S. no.	MAP_75	MAP_90	MAP_105	MAP_120	MAP_150	MAP_180	SpO2_Baseline	SpO2_0	SpO2_2	SpO2_4	SpO2_6	SpO2_8	SpO2_10	SpO2_15	SpO2_30	SpO2_45	SpO2_60	SpO2_75	SpO2_90	SpO2_105	SpO2_120	SpO2_150	SpO2_180	SL_Baseline	SL_0	SL_2	SL_4	SL_6	SL_8	SL_10
1	90						100	100	100	100	100	100	100	100	100	100	100	100							L4	L2	T11	T10	T9
2	77	89	88	88	89	89	100	100	99	98	100	100	100	100	100	100	100	100	100	100	100	100		S2	L1	T12	T9	T6	T6
3	110	112					97	98	98	98	97	98	98	98	99	98	99	99	99						T12	T8	T6	T6	T6
4	73	73	76	81	96		98	97	98	98	97	98	97	98	99	100	100	100	100	99	100	100		L4	T12	T10	T6	T6	T6
5	77						100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100		T12	T10	T9	T8	T6	T6
6	85	92								99	98	99	100	99	99	99	99	99	99					S1	L4	L2	T12	T10	T6
7							98	97	98	98	98	98	98	98	100	100										L4	T10	T8	T6
8																													
9	100	99	108	105			98	98	98	100	99	99	99	100	100	100	100	100	100	100	100				0	T10	T6	T4	T4
10																													
11	82	72	78	84	85	92	97	97	97	97	98	97	97	97	96	100	97	99	98	99	99	100	100		T12	T8	T8	T8	T6
12	82	92					98	98	97	98	97	98	98	99	99	99	98	98	99					S1	L5	L4	L2	T10	T8
13							99	99	99	99	99	99	99	100	100	100									T10	T10	T8	T6	T4
14	67	71					94	94	93	94	95	97	98	97	97	95	98	98	98						T12	T12	T10	T8	T6
15	102	104	100	100	100		96	98	98	98	97	99	99	99	100	100	100	100	100	100	100	100			L4	T12	T8	T8	T8
16							100	100	100	100	100	100	100	100	100										L5	L2	T12	T10	T10
17	97						97	98	100	99	99	100	98	98	95	99	100	100							T12	T10	T8	T6	T3
18							98	100	100	100	99	99	99	94	98	96	98								T10	T9	T5	T4	T4
19	78	93	94	98			100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				L1	T12	T12	T12	T12
20	96						100	100	100	100	100	100	100	98	97	97	99	100							L4	T12	T4	T4	T4
21	71	82	82	86	82		97	99	99	99	99	99	100	100	100	100	99	98	98	100	100	100				L2	T12	T10	T10
22							100	100	99	99	100	100	100	100	100	100	100									T12	T12	T10	T10
23	82	84	87				100	99	100	99	100	100	100	100	100	100	100	100	100	100					L5	T12	T10	T8	T6
24							100	100	98	97	99	100	100	100	100	100	98									T12	T12	T12	T12
25							100	100	100	100	100	100	100	100	100	100									L2	T12	T10	T8	T6
26	82	84	86	104	95		96	96	97	97	96	97	96	98	95	95	96	95	95	95	96	94			L5	T10	T8	T8	T8
27	123						100	100	100	100	100	100	100	100	99	99	99	99							L2	T12	T12	T10	T10
28							98	98	98	98	98	97	97	97	98										T12	T12	T10	T8	T4
29	80	82	82	80	80		100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100			T12	T12	T12	T12	T10
30	114						99	99	98	98	98	98	99	98	99	99	99	99							L2	L2	L2	L1	T12
31	90	89	92	94	92	90	100	100	100	100	100	100	100	100	99	98	96	98	98	97	98	98	98		L4	L1	T12	T12	T12
32	82	86	84	82			98	98	98	99	99	98	99	97	97	99	99	99	99	99	99			S1	T12	T10	T10	T6	T6
33	90	91	86				100	100	100	100	100	100	100	100	100	100	100	100	98	98						L1	T11	T10	T10
34	97	99	99	114	102	106	100	100	100	100	100	100	100	100	100	100	99	100	100	100	100	100	100		L2	T10	T10	t10	T8
35	94						100	100	100	100	100	100	100	100	100	100	100	100						L2	T12	T10	T8	T6	T5
36	100						98	99	100	100	100	100	100	100	100	100	100	100							T12	T10	T10	T8	T8
37							100	100	100	100	100	100	100	100												L5	L2	L2	L2
38	78	80					100	100	98	97	97	98	99	96	97	97	98	97	97						T12	T10	T8	T6	T4
39	110						95	94	94	98	98	99	99	99	100	100	100	100							L2	T12	T12	T11	TI0
40							100	100	100	100	100	100	100	100	100	100	100									L2	T12	T12	T11
41	104	100	102	100			98	98	98	98	99	99	99	99	99	99	99	99	99	98	98					L4	L4	L2	T12
42							99	99	99	99	99	99	99	99	99	99									L4	L2	T12	T11	T10
43	100	90	92				100	100	100	99	100	100	99	99	99	100	100	100	100	100					L1	T12	T10	T10	T8
44	107	125	124	121	120		97	98	98	98	98	98	97	97	98	98	98	98	98	97	98	97					S1	L1	L1
45	90	98					98	97	98	98	98	98	98	97	97	97	98	97	97							T10	T8	T8	T6
46	97	89	100	95			100	100	100	100	100	100	100	100	100	96	98	98	98	98	98				L1	T11	T8	T8	T8
47	88	89					100	100	100	100	100	100	99	99	98	96	98	96	97						T12	T12	T10	T10	T10
48							97	97	99	98	98	98	98	98	99	97	99								T12	T10	T8	T8	T8
49	97	85	95				98	98	97	97	98	99	97	100	99	99	98	98	98	98					T12	T10	T8	T8	T8
50							96	98	99	99	98	98	97	99	98	98	98								L1	T12	T11	T11	T10
51	110	102	99	106			100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				T12	T10	T10	T6	T6
52	80	84	84				99	99	98	99	99	99	97	97	98	98	98	98	98	98					T12	T10	T8	T6	T5
53							100	100	100	100	100	100	100																
54	83	90					100	100	99	100	100	100	100	100	99	99	98	99	99							T12	T10	T10	T8
55							100	100	100	100	100	100	98	99	98										S1	T10	T10	T8	T6
56	109	108					100	100	100	100	100	99	98	100	100	100	100	99	100						L2	T12	T10	T8	T6
57	85	90	90	89	94		97	100	100	100	100	100	100	96	97	97	100	100	100	100	100	100			T12	T10	T8	T6	T4
58	82	93	96	90			100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				T12	T6	T6	T6	T6
59	110	102	99	99	101		100	100	100	100	100	100	100	100	100	100	100	100	100	100	100				T12	T10	T10	T6	T6
60							98	97	97	97	97	98	99	99	97	97	97								T6	T4	T4	T4	T4
61	98						99	97	98	100	100	100	100	99	99	99	98	98							L1	T10	T10	T8	T8
62	89	88	87				100	100	100	100	100	100	100	100	100	100	100	100	100	100					T12	T10	T8	T6	T6
63							97	96	96	94	94	94	95	96	96	97	97								L3	L1	T12	T10	T8
64	88						96	96	97	96	97	96	98	98	98	98	98	100							L1	T12	T8	T8	T8

S. no.	SL_15	SL_30	SL_45	SL_60	SL_75	SL_90	SL_105	SL_120	SL_150	SL_180	MBS_Baseline	MBS_0	MBS_2	MBS_4	MBS_6	MBS_8	MBS_10	MBS_15	MBS_30	MBS_45	MBS_60	MBS_75	MBS_90	MBS_105	MBS_120	MBS_150	MBS_180	Vasopressor_Baseline	Vaso_0	Vaso_2	Vaso_4	Vaso_6
1	T8	T8	T8	T8	T8								2	2	3																	
2	T6	T6	T6	T6	T6	T8						1	3																			6mg
3	T6	T6	T6	T6	T6	T8							2	3							3	3	2									
4	T4	T4	T4	T4	T4	T5	T6	T8				1	3	3											3	2						6 mg
5	T6	T6	T6	T6	T6							2	2	3								2										
6	T4	T4	T4	T4	T5	T6						1	2	3	3																	
7	T6	T6	T6													1	2	3	3	3												
8																																
9	T3	T3	T3	T3	T3	T4	T6	T6					1	2	2	3							2	1	0							
10																																
11	T6	T6	T6	T6	T6	T8						1	2	3													0					
12	T8	T8	T8	T8	T9	T11							1	2	2	2	3															
13	T4	T4	T4										2	3																		
14	T6	T6	T6	T6	T6	T8							2	2	3	3																
15	T6	T6	T6	T6	T6	T6	T8						0	3											3	0						
16	T8	T8											0	1	2	2	2	3														
17	T3	T3	T4	T5	T5							0	1	3																		
18	T4	T4	T4	T4									3																			6 mg
19	T10	T10	T10	T10	T10	T10	T10	T12					1	2	2	2	2	3	3						3							
20	T3	T3	T3	T3	T3								1	3	3																	6mg
21	T10	T8	T8	T8	T8	T10							0	0	2	2	3															
22	T10	T10	T10	T10										1	2	2	2	3	3													
23	T4	T4	T4	T4	T4	T4	T6						2	3																		
24	T10	T6	T6	T6									1	2	3																	
25	T6	T6	T8									0	1	2	3																	
26	T6	T4	T4	T4	T4	T5	T6						1	2	3											2						6 mg
27	T10	T10	T10	T10	T12								2	3								3										
28	T4	T4											2	3																		
29	T10	T10	T10	T10	T10	T12							2	3																		
30	T10	T8	T8	T10	T10								1	1	1	2	2	3														
31	T10	T8	T8	T8	T8	T8	T10					0	1	3	3																	
32	T5	T4	T4	T4	T5	T5	T5	T6				1	3																			
33	T8	T6	T6	T6	T6	T8								1	2	3																
34	T6	T4	T4	T4	T4	T4	T4	T6					2	3																		
35	T5	T5	T5	T5	T8							0	2	3																		
36	T6	T6	T6	T6	T6								1	2	3																	
37	L2												0	1	2	2	2	2														
38	T4	T4	T4	T4	T5	T6							2	3																	6 mg	12mg
39	T10	T10	T10	T10	T12								2	3																		
40	T10	T10	T10	T11										1	2	2	2	3	3	3	3											
41	T10	T10	T10	T10	T12									1	1	2	3	3														
42	T8	T8	T10										0	1	1	2	3															
43	T8	T8	T8	T8	T8	T10							2	3	3																	
44	T12	T10	T8	T8	T8	T10	T10	T12						1	2	3																
45	T4	T4	T4	T4	T4	T6																										
46	T8	T6	T6	T6	T7	T8	T10	T10					2	3																		
47	T8	T6	T6	T8	T8								2	3																		
48	T6	T6	T6	T6									2	3																		
49	T6	T6	T6	T6	T7	T8							2	3																		
50	T10	T10	T10	T10									2	3	3																	
51	T5	T5	T5	T5	T5	T8	T8	T10					3																			
52	T5	T5	T5	T6	T8	T10	T12						3																			
53																																
54	T6	T6	T6	T6	T6	T8							1	2	3																	
55	T6	T6											0	3																		
56	T6	T6	T6	T6	T7	T8							2	3																		
57	T4	T4	T4	T4	T5	T6							2	3																	6 mg	
58	T6	T6	T6	T6	T6	T8							3																			
59	T5	T5	T5	T5	T6	T8							3																			
60	T4	T4	T4	T4									2	3																		
61	T8	T8	T8	T8	T8								1	3																		
62	T4	T4	T4	T4	T4	T5							3																			
63	T8	T8	T8	T8									1	2	3																	
64	T6	T4	T4	T4	T4								2	3	3	3																

S. no.	Vaso_8	Vaso_10	Vaso_15	Vaso_30	Vaso_45	Vaso_60	Vaso_75	Vaso_90	Vaso_105	Vaso_120	Vaso_150	Vaso_180	SBP_1	SBP_2	SBP_3	DBP_1	DBP_2	DBP_3	MAP_1	MAP_2	MAP_3	1	2	3	SBP_1	SBP_2	SBP_3	DBP_1	DBP_2	DBP_3	MAP_1	MAP_2	MAP_3
1																																	
2		6mg											74	90		50	60		57	68		6mg	6mg		106	119		80	47		90	96	
3																																	
4					6 mg								87	82		51	54		64	64		6 mg	6 mg		98	99		54	58		68	72	
5																																	
6				6 mg									100			65			81			6 mg			104			72			84		
7																																	
8																																	
9																																	
10																																	
11																																	
12			6 mg										101	98		86	60		80	54		6 mg	6 mg		109	110		68	70		80	82	
13		6 mg											100	124		60	70		72	94		6 mg	6 mg		124	150		70	80		94	103	
14		6 mg				6 mg							88	85		33	32		54	60		6 mg	6mg		96	99		50	52		64	68	
15																																	
16																																	
17			6 mg	6 mg									103	105	107	60	60	65	78	78	79	6 mg	6mg	6 mg	120	124	128	82	82	80	96	98	99
18	6 mg	6 mg		6 mg + 6 mg									90	82	88	35	38	39	56	58	60	6 mg	6 mg	6 mg	82	88	108	38	39	59	58	60	74
19																																	
20	6 mg	6 mg	6 mg										115	105	107	72	67	66	87	80	84	6 mg	6 mg	6 mg	115	114	112	70	74	67	86	86	88
21						6 mg	6 mg						94	92		55	59		68	71		6 mg	6 mg		101	104		60	66		74	79	
22																																	
23						6 mg							108	108		60	62		79	80		6 mg	6 mg		113	118		64	66		84	85	
24																																	
25																																	
26			6 mg	6 mg									88	89	88	58	57	57	66	67	67	6 mg	6mg	6 mg	116	101	109	69	66	62	83	77	83
27																																	
28																																	
29																																	
30																																	
31																																	
32													106	102	106	61	55	55	78	76	77	6mg	6 mg	6mg	112	110	110	64	61	62	82	78	81
33																																	
34																																	
35																																	
36													108			72			84			6mg			117			78			89		
37																																	
38			6 mg										80	70	97	40	30	54	53	43	68	6 mg	12 mg	6 mg	70	101	104	30	61	67	43	78	79
39																																	
40																																	
41																																	
42																																	
43																																	
44																																	
45		6 mg	6 mg			6 mg		6 mg					120	106	116	60	52	66	80	70	83	6 mg	6 mg	6 mg	134	136	140	64	66	70	87	89	93
46						6 mg	6 mg	6 mg					126	103	126	77	70	80	97	81	105	6 mg	6 mg	6 mg	143	126	135	78	80	80	102	105	100
47				6 mg									92	95	92	58	58	59	72	75	72	6 mg	6 mg	6 mg	110	122	120	67	64	66	83	93	93
48		6 mg	6 mg										92	110	126	61	74	81	72	87	94	6 mg	6 mg	6 mg	105	126	141	72	81	91	84	94	107
49																																	
50																																	
51																																	
52													94			60			78			6 mg			111			73			83		
53																																	
54																																	
55																																	
56																																	
57	6 mg												96	98		47	50		68	74		6 mg	6 mg		96	118		50	60		72	80	
58																																	
59																																	
60																																	
61																																	
62			6 mg										90	90		40	50		57	63		6 mg	6 mg		114	124		70	68		85	87	
63													102			55			73			6 mg			123			64			87		
64																																	

S. no.	Maximum sensory level attained	Amount of vasopressor needed to treat hypotension	Total amount of I.V. fluids administered	Episodes of Hypotension (Y/N)	Episodes of Bradycardia	HR_0	HR_30	HR_60	HR_90	HR_120	HR_150	HR_180	HR_210	HR_240	HR_270	HR_300	HR_330	HR_360	SBP_0	SBP_30	SBP_60	SBP_90	SBP_120	SBP_150	SBP_180	SBP_210	SBP_240	SBP_270
1	T8		1000 ml	N	N	70	60	64	70	68	67	66	70	72	74	70	68	66	126	124	120	118	114	124	128	130	132	124
2	T6	12mg	1200ml	Y	N	116	90	82	76	78	79	82	84	86	82	80	82	86	128	120	116	114	116	112	116	120	128	128
3	T6		800ml	N	N	82	84	88	90	76	72	68	86	96	86	84	80	82	142	144	142	148	150	160	142	140	148	142
4	T4	12 mg	2200 ml	Y	N	90	92	90	89	86	84	86	84	88	92	90	90	92	124	126	120	124	126	130	132	130	128	126
5	T6		1000ml	N	N	63	69	72	70	72	74	76	78	76	78	80	82	84	108	110	120	124	120	118	124	126	124	120
6	T4	6 mg	1100 ml	Y	N	96	100	102	100	101	98	92	94	96	98	98	94	92	116	120	124	126	130	132	136	130	128	132
7	T6		1000ml	N	N	79	82	80	90	82	86	88	90	92	88	86	84	86	124	130	126	136	138	130	132	134	130	128
8																												
9	T3		1500 ml	N	N	54	58	56	58	68	54	56	57	56	54	55	55	58	132	134	130	132	148	134	146	142	138	140
10																												
11	T6		2000 ml	N	N	85	86	88	92	90	90	92	94	96	88	92	87	94	131	132	138	140	142	140	138	138	142	138
12	T8	12 mg	1200 ml	Y	N	100	102	104	102	108	110	111	109	108	108	104	110	106	140	140	142	138	142	138	140	140	138	136
13	T4		1000 ml	Y	N	80	82	76	72	78	74	76	80	82	78	80	76	84	120	126	124	128	126	124	130	126	126	132
14	T6	12mg	2000 ml	Y	N	110	94	98	100	108	111	100	98	94	98	95	94	98	101	110	110	112	116	114	112	116	114	112
15	T6		1500 ml	N	N	87	89	88	80	87	82	85	80	86	78	89	79	88	134	136	130	128	132	126	134	130	132	126
16	T8		500 ml	N	N	71	67	73	80	82	78	82	80	84	78	82	84	86	130	138	140	144	146	148	144	140	146	140
17	T3	18 mg	1600 ml	Y	N	82	86	84	82	84	82	82	83	88	90	84	90	86	124	128	130	128	132	134	132	136	132	128
18	T4	30 mg	2000 ml	Y	N	94	95	98	100	106	98	104	99	106	102	98	104	100	115	105	118	120	120	124	120	122	118	120
19	T10		1600 ml	N	N	116	120	114	120	118	122	116	118	114	116	116	112	118	130	128	126	130	128	132	128	132	130	134
20	T3	30 mg	1100 ml	Y	N	81	80	82	84	88	82	84	86	86	80	88	82	86	128	130	130	134	132	134	130	128	134	140
21	T8	12 mg	2000 ml	Y	N	94	93	90	92	96	90	92	94	98	92	90	94	92	110	116	120	118	120	124	126	124	130	130
22	T10		1100 ml	N	N	104	95	98	96	94	98	95	100	97	102	98	92	99	109	120	110	116	114	118	120	124	118	122
23	T4	12 mg	1500 ml	Y	N	89	84	88	90	82	84	88	86	89	90	90	92	94	120	124	122	126	120	116	118	124	118	122
24	T6		1000 ml	N	N	68	72	74	70	72	68	68	77	70	76	72	70	74	116	114	112	116	114	120	116	112	118	118
25	T6		1200 ml	N	N	103	100	104	102	104	106	104	100	102	101	101	100	98	142	140	142	138	140	130	132	128	130	132
26	T4	24 mg	1200 ml	Y	N	73	79	82	84	80	82	86	82	84	86	88	84	86	160	150	154	160	152	156	154	156	154	152
27	T10		750 ml	N	N	100	88	90	92	94	92	90	98	94	95	92	94	95	154	150	145	144	140	142	146	148	147	150
28	T4		600 ml	N	N	70	74	72	70	74	76	72	78	74	76	78	79	80	110	110	114	116	114	118	116	114	120	124
29	T10		1500 ml	N	N	81	84	82	86	84	84	85	89	86	84	86	85	89	100	102	104	102	100	102	104	102	100	102
30	T8		1000 ml	N	N	84	86	88	86	84	90	86	88	89	94	92	96	94	150	146	144	140	138	142	136	134	136	140
31	T8		1400 ml	N	N	60	61	62	64	63	68	60	64	59	62	58	66	60	120	118	116	120	116	122	118	126	124	128
32	T4	18 mg	1500 ml	Y	N	100	102	108	104	108	112	110	116	112	110	114	110	116	120	124	126	124	122	128	130	132	128	134
33	T6		1200 ml	N	N	72	74	89	80	86	84	82	86	80	88	84	82	82	110	112	120	124	116	122	118	124	120	128
34	T4		1500 ml	N	N	82	84	86	84	86	80	78	82	89	84	92	94	90	140	142	149	148	130	132	138	142	146	146
35	T5		800 ml	N	N	86	89	100	92	98	96	92	99	94	98	89	96	92	124	130	128	134	128	136	130	132	129	134
36	T6	6mg	1100 ml	Y	N	80	82	84	86	84	88	82	80	84	90	82	89	80	120	124	128	132	134	138	130	140	132	138
37																												
38	T4	42 mg	1600 ml	Y	N	110	108	110	112	100	110	108	105	102	103	104	109	102	110	112	114	110	116	128	118	130	124	118
39	T10		600 ml	N	N	70	71	68	69	68	76	67	70	68	62	70	78	72	140	142	150	154	160	150	160	164	162	154
40	T10		700 ml	N	N	68	72	74	72	74	80	73	82	74	72	78	71	80	120	124	122	130	126	120	130	136	120	130
41	T10		2000 ml	N	N	70	68	69	70	72	74	70	64	62	63	64	68	66	140	146	142	140	138	140	142	146	144	138
42	T8		900 ml	N	N	93	94	92	93	94	92	94	96	93	97	90	93	89	124	124	130	128	128	124	132	128	130	132
43	T8		1100 ml	N	N	64	60	62	66	63	64	65	62	63	68	67	62	64	130	132	134	130	128	132	136	130	128	126
44	T8		1800 ml	N	N	55	60	62	64	66	65	62	64	66	62	66	62	70	160	162	164	158	168	158	162	170	170	166
45	T4	24 mg	2000 ml	Y	N	62	64	64	66	66	62	70	71	72	70	68	70	62	116	114	120	120	124	130	134	136	142	140
46	T6	30 mg	1500 ml	Y	N	88	82	86	84	89	90	86	92	94	92	89	90	92	142	168	160	164	170	168	172	166	162	160
47	T6	24 mg	1300 ml	Y	N	80	82	78	81	80	80	80	82	82	84	86	80	78	112	110	112	119	124	130	132	130	130	134
48	T6	30 mg	1500 ml	Y	N	112	108	104	102	104	103	104	106	118	110	104	116	112	110	120	130	134	140	142	146	142	150	148
49	T6		1200 ml	N	N	83	80	80	80	82	84	90	80	78	82	76	84	72	124	110	100	104	110	110	126	118	120	116
50	T10		700 ml	N	N	80	82	84	89	90	90	84	82	76	78	82	80	84	112	114	120	118	116	110	112	116	120	124
51	T5		1300 ml	N	N	78	79	80	76	70	74	72	76	80	82	80	84	80	126	120	124	122	126	128	120	124	124	120
52	T5		1500 ml	Y	N	69	70	68	70	66	67	68	66	69	70	72	73	78	114	112	114	116	112	110	116	114	112	118
53																												
54	T6		1200 ml	N	N	70	70	74	76	70	72	80	78	82	79	80	78	76	116	114	116	120	118	116	114	120	124	128
55	T6		1000 ml	N	N	87	81	80	82	84	86	80	82	81	86	87	88	89	108	100	102	100	104	110	108	110	112	110
56	T6		1200 ml	N	N	70	72	69	70	72	74	80	88	79	89	78	70	68	128	120	114	116	112	120	122	124	126	138
57	T4	12 mg	2000 ml	Y	N	82	84	79	78	86	84	90	88	89	92	94	92	96	128	130	132	130	126	134	140	132	142	138
58	T6		1600 ml	N	N	86	90	92	90	89	94	96	92	90	89	88	92	96	124	128	130	132	130	128	130	126	134	138
59	T5		1500 ml	N	N	78	80	82	78	76	74	72	76	80	82	84	80	82	126	120	124	128	126	134	130	130	126	128
60	T4		1000 ml	N	N	70	73	76	74	80	78	76	82	80	84	76	78	82	105	110	109	110	112	110	114	118	62	118
61	T8		800 ml	N	N	63	64	75	70	68	72	76	66	68	70	74	76	72	130	134	136	130	140	138	142	146	150	142
62	T4	12 mg	1800 ml	Y	N	89	86	89	90	92	90	84	86	82	83	87	91	89	126	122	120	116	124	118	126	130	128	132
63	T8	6 mg	1200 ml	Y	N	62	60	64	70	72	68	64	67	66	62	64	68	67	110	112	116	114	109	110	118	120	124	130
64	T4		1000 ml	N	N	69	62	68	63	66	72	71	69	70	74	70	68	67	131	132	134	136	142	140	138	140	132	134

S. no.	SBP_300	SBP_330	SBP_360	DBP_0	DBP_30	DBP_60	DBP_90	DBP_120	DBP_150	DBP_180	DBP_210	DBP_240	DBP_270	DBP_300	DBP_330	DBP_360	MAP_0	MAP_30	MAP_60	MAP_90	MAP_120	MAP_150	MAP_180	MAP_210	MAP_240	MAP_270	MAP_300	MAP_330	MAP_360
1	120	128	130	72	70	70	68	70	78	80	80	82	70	70	80	80	90	89	87	88	86	89	90	92	90	89	87	90	92
2	133	130	132	82	80	79	79	79	69	70	80	82	80	75	80	76	89	90	89	88	89	88	89	90	89	88	101	104	100
3	144	140	144	82	80	84	90	90	100	86	80	80	82	80	80	80	110	112	113	112	110	109	110	109	108	113	112	109	112
4	124	120	124	76	80	72	74	76	84	82	80	80	78	74	72	76	96	94	88	91	93	99	99	98	96	94	91	88	96
5	122	124	120	73	70	72	76	72	70	72	74	72	80	74	76	70	86	86	89	92	88	86	89	91	89	93	90	92	87
6	136	128	130	70	71	76	80	70	76	84	78	80	80	78	74	82	89	90	92	94	96	95	101	95	96	97	97	92	98
7	130	134	132	98	100	98	100	104	100	98	102	100	92	100	102	100	109	112	109	114	115	110	109	113	110	104	110	113	111
8																													
9	142	138	144	80	82	80	82	90	83	89	89	80	86	88	80	90	94	95	92	93	102	94	100	93	92	98	93	92	100
10																													
11	144	142	140	88	89	89	90	90	90	80	82	89	80	92	90	90	109	110	110	110	111	110	110	110	112	110	114	111	109
12	132	136	138	78	80	82	80	86	82	78	82	82	84	78	80	82	95	95	96	94	96	94	95	96	94	96	89	95	94
13	124	130	125	70	74	72	76	74	72	78	80	80	80	80	78	79	94	95	92	96	94	93	98	96	95	99	93	98	92
14	116	114	112	77	80	70	74	80	76	74	80	80	74	82	80	78	78	82	80	84	82	80	82	86	84	82	82	84	82
15	130	128	136	80	82	80	78	82	78	86	80	84	80	80	80	84	102	104	100	98	100	98	102	100	101	96	100	98	104
16	150	142	148	85	83	89	90	92	94	94	86	95	88	96	89	96	99	100	100	100	102	106	102	100	102	101	108	102	106
17	134	130	134	84	86	90	89	89	92	90	94	90	89	92	90	94	100	101	104	102	106	107	105	108	102	101	104	105	105
18	124	118	122	66	64	70	72	80	82	80	82	78	80	82	78	82	74	71	76	78	88	89	88	88	84	88	89	84	88
19	124	130	120	80	76	74	80	76	82	78	80	80	84	74	80	70	104	100	98	104	99	106	98	104	100	106	94	104	92
20	132	140	138	84	80	80	84	82	84	80	84	84	88	82	90	86	97	98	98	99	99	99	98	97	99	102	98	104	104
21	128	126	128	70	72	80	70	82	84	82	84	90	90	84	82	84	75	76	80	78	82	84	86	84	86	87	84	82	84
22	120	112	116	70	74	65	68	68	68	72	76	70	74	74	66	68	84	93	86	89	88	89	92	96	90	94	94	86	89
23	120	124	124	70	72	70	74	70	66	68	72	68	68	70	76	72	88	89	88	89	86	82	85	88	84	82	89	89	90
24	120	126	124	69	68	62	64	68	72	69	62	70	66	72	76	74	86	84	82	86	84	90	86	82	88	88	90	94	92
25	134	132	134	78	80	82	80	82	80	81	79	80	82	84	82	84	93	92	94	90	92	85	86	82	84	84	86	84	86
26	154	156	160	86	80	84	90	82	86	84	86	84	82	84	86	90	111	105	107	110	108	109	108	109	108	104	108	110	112
27	152	148	146	94	90	97	98	94	85	98	100	98	100	100	98	96	110	108	99	100	98	102	104	106	107	110	112	98	97
28	120	118	118	70	70	74	74	76	74	72	74	80	82	80	79	78	82	82	84	84	86	86	84	84	90	92	90	89	89
29	102	104	104	70	74	72	72	70	72	74	74	70	72	74	72	72	80	82	83	82	80	81	82	81	80	81	84	83	82
30	132	138	134	98	94	92	90	89	90	86	84	86	90	84	89	86	120	114	112	110	108	110	104	102	104	110	100	108	104
31	120	124	122	70	68	70	72	68	70	70	72	74	76	72	74	70	90	88	85	92	86	92	88	92	94	96	92	94	92
32	124	130	120	80	82	84	82	80	86	90	92	86	94	84	90	82	92	94	96	92	94	96	98	99	96	101	94	98	92
33	124	126	120	68	70	78	82	74	80	78	82	80	86	82	84	80	87	88	92	94	89	92	90	94	92	96	94	96	92
34	140	144	142	82	84	90	89	78	79	80	84	84	88	82	86	80	101	103	110	109	95	97	99	103	105	108	101	106	101
35	124	128	126	70	90	84	92	88	94	90	90	88	92	82	84	80	94	103	99	106	101	108	103	104	102	106	96	99	95
36	130	142	132	80	84	84	82	84	88	82	90	84	88	82	92	84	100	102	102	104	108	110	106	114	106	110	102	116	104
37																													
38	124	114	130	66	68	70	70	68	86	70	90	82	70	84	70	90	82	84	84	82	86	96	90	97	92	90	94	84	97
39	158	162	160	89	92	98	100	108	98	106	108	110	100	104	110	108	110	109	115	118	125	115	124	125	127	118	122	127	125
40	124	128	128	82	84	82	90	86	82	90	94	82	90	84	90	88	95	97	95	103	99	95	103	108	95	103	97	103	102
41	140	146	138	82	89	80	82	82	82	80	89	82	82	82	89	80	104	109	106	104	102	104	106	109	108	102	104	109	100
42	132	128	134	76	72	78	76	78	72	80	78	82	80	80	78	78	95	94	96	97	96	94	97	96	98	97	97	96	97
43	128	130	134	74	76	74	70	68	72	74	72	66	62	68	72	74	93	95	94	90	88	92	95	91	87	83	88	91	94
44	164	162	164	100	102	100	98	104	96	100	108	106	102	104	102	100	120	122	121	118	125	117	121	129	127	123	124	122	121
45	142	138	140	66	66	70	70	72	78	78	80	84	82	80	78	78	83	82	87	87	89	95	97	99	103	101	101	98	99
46	158	158	160	78	90	90	92	92	94	92	86	82	80	82	80	86	99	116	113	116	118	119	119	113	109	107	107	106	111
47	128	132	132	75	74	76	84	84	86	90	84	88	86	84	84	88	85	84	88	104	97	101	104	99	102	102	109	100	102
48	152	148	150	70	70	76	78	80	82	84	86	90	90	92	88	92	73	87	94	97	100	102	104	103	108	106	112	104	110
49	118	122	124	71	72	73	70	72	74	74	72	72	70	70	74	74	91	88	86	81	88	89	94	89	91	88	90	92	92
50	118	120	116	70	72	76	74	70	68	70	72	80	82	78	76	70	84	86	91	89	85	82	84	87	93	96	91	91	85
51	122	128	130	76	70	72	74	76	74	70	72	74	70	74	76	80	93	87	89	90	93	92	87	89	91	87	90	93	97
52	126	112	120	74	72	74	76	74	70	72	74	72	70	82	80	80	78	76	78	79	78	74	76	76	74	78	82	78	82
53																													
54	126	120	122	78	67	70	74	70	68	70	82	84	88	82	84	80	89	81	85	89	86	84	85	95	97	101	97	96	94
55	108	106	110	56	51	54	52	54	58	56	60	64	60	58	54	58	71	67	70	68	71	75	73	77	80	77	75	71	75
56	120	124	126	86	80	76	78	72	80	82	84	84	92	80	82	84	100	93	91	91	85	93	95	97	98	107	93	96	98
57	132	140	136	82	84	82	80	78	86	0	88	90	90	82	86	90	97	99	99	97	94	102	107	103	107	106	99	104	105
58	140	124	130	76	86	86	86	84	84	86	84	86	90	90	76	86	92	96	101	102	100	95	101	94	102	106	107	92	101
59	124	128	130	76	70	72	74	76	80	78	76	76	74	72	74	76	93	87	89	92	93	102	100	100	93	92	89	92	100
60	116	114	118	72	73	72	72	76	72	76	74	82	76	80	80	74	83	87	85	85	87	85	86	88	92	89	87	86	88
61	146	144	150	76	78	74	80	82	86	90	89	90	86	84	86	89	93	97	95	97	101	103	107	108	110	105	105	105	109
62	134	130	124	72	70	68	68	72	70	76	80	78	84	86	90	82	90	87	85	84	89	86	93	97	95	100	102	103	96
63	132	128	132	60	62	64	62	58	58	66	70	70	82	80	76	84	77	79	81	79	75	75	83	87	88	98	97	93	100
64	140	146	150	65	68	70	72	74	70	68	72	62	64	74	78	80	88	89	91	93	97	93	91	95	85	87	96	101	103

S. no.	SpO2_0	SpO2_30	SpO2_60	SpO2_90	SpO2_120	SpO2_150	SpO2_180	SpO2_210	SpO2_240	SpO2_270	SpO2_300	SpO2_330	SpO2_360	SL_0	SL_30	SL_60	SL_90	SL_120	SL_150	SL_180	SL_210	SL_240	SL_270	SL_300	SL_330	SL_360	MBS_0	MBS_30	MBS_60	MBS_90	MBS_120
1	100	100	100	100	100	100	100	100	100	100	100	100	100	T8	T10												3	2	1	0	
2	100	100	100	100	100	100	100	100	100	100	100	100	100														3	2	0		
3	99	98	99	98	98	97	98	99	99	99	99	99	99														0				
4	100	100	100	100	100	100	100	100	100	100	100	100	100														2	0			
5	100	100	100	100	100	100	100	100	100	100	100	100	100	T8													2	1	0		
6	99	99	99	99	99	99	99	99	99	99	99	99	99														3	2	1	0	
7	100	100	100	100	100	100	100	100	100	100	100	100	100	T6	T8												2	0	0		
8																															
9	100	100	100	100	100	100	100	100	100	100	100	100	100																		
10																															
11	97	98	98	98	99	99	99	99	99	99	99	99	99																		
12	96	96	97	96	96	97	97	96	97	97	97	97	97														3	3	2	0	
13	100	100	100	100	100	100	100	100	100	100	100	100	100	T4	T6												3	3	3	2	2
14	95	95	98	98	99	98	97	98	99	98	98	99	99														3	0			
15	100	100	100	100	100	100	100	100	100	100	100	100	100																		
16	100	100	100	100	100	100	100	100	100	100	100	100	100	T8	T8	T10											3	3	2	1	0
17	100	100	100	100	100	100	100	100	100	100	100	100	100														3	3	3	3	2
18	95	99	96	97	97	97	97	97	98	98	97	98	97	T4	T6												3	3	2	1	0
19	100	100	100	100	100	100	100	100	100	100	100	100	100														3	2	1	0	
20	100	100	100	100	100	100	100	100	100	100	100	100	100	T4	T5												3	3	3	2	1
21	100	100	100	100	100	100	100	100	100	100	100	100	100														0				
22	100	100	100	100	100	100	100	100	100	100	100	100	100	T11	T12												1	0			
23	100	100	100	100	100	100	100	100	100	100	100	100	100														3	2	1	0	
24	98	97	98	98	99	99	98	98	98	98	99	98	98														3	3	3	2	1
25	100	100	100	100	100	100	100	100	100	100	100	100	100	T10													3	2	1	0	
26	96	94	95	96	95	94	94	95	96	95	94	95	96														0				
27	100	100	100	100	100	100	100	100	100	100	100	100	100														3	2	2	0	
28	98	98	99	99	99	100	100	100	98	98	98	100	99	T4	T4	T6											3	3	3	2	1
29	100	100	100	100	100	100	100	100	100	100	100	100	100														3	1	0		
30	99	99	99	99	99	99	99	99	99	99	99	99	99														1	0			
31	98	98	97	99	98	98	98	98	98	98	98	98	98														2	1	0	0	
32	98	99	99	98	99	99	98	98	99	99	98	98	99														3	3	2	1	0
33	100	100	100	100	100	100	100	100	100	100	100	100	100														0				
34	100	100	100	100	100	100	100	100	100	100	100	100	100														0				
35	100	100	100	100	100	100	100	100	100	100	100	100	100														2	1	0		
36	100	100	100	100	100	100	100	100	100	100	100	100	100	T6	T10												3	2	1	0	
37																															
38	98	99	98	99	99	99	100	100	100	100	100	99	100														3	3	2	1	0
39	100	100	99	98	99	99	98	98	98	98	98	98	98	T12													3	3	2	1	0
40	100	100	100	100	100	100	100	100	100	100	100	100	100	T11	T12												2	1	0		
41	98	98	99	99	98	99	98	98	99	98	98	98	98														1	0			
42	100	100	100	100	100	100	100	100	100	100	100	100	100	T10													3	3	2	2	2
43	100	100	100	100	98	99	99	99	100	100	100	99	99														2	2	1	0	
44	97	98	97	99	98	97	97	97	98	97	98	97	97														1	0			
45	97	97	97	97	98	98	98	98	98	97	98	98	98	T6	T8												3	3	2	1	0
46	98	99	98	98	99	99	99	100	100	100	99	99	99														1	0			
47	100	100	100	98	100	99	99	99	99	99	99	99	99														3	3	3	2	2
48	100	100	100	100	100	100	100	100	99	99	98	99	99	T6	T6	T8											3	3	3	3	2
49	98	100	99	99	99	99	98	98	98	98	98	98	98	T8	T10												3	2	1	0	
50	100	98	99	98	99	100	100	100	98	99	98	99	99	T10	T10	T12											3	3	3	2	1
51	100	100	100	100	100	100	100	100	99	99	99	100	100														3	2	1	0	
52	99	98	99	99	99	98	99	99	98	98	99	99	99														3	3	2	2	2
53																															
54	100	100	100	100	100	99	100	100	99	99	100	100	100														1	0			
55	98	97	97	98	98	98	97	98	98	98	98	98	98	T6	T6	T8											3	3	3	2	1
56	99	99	98	99	98	99	100	99	100	100	100	99	98														3	3	3	2	2
57	100	100	100	100	100	100	100	100	100	100	100	100	100														2	1	0		
58	100	100	100	100	100	100	100	100	100	100	100	100	100														3	3	2	2	1
59	100	100	100	100	100	100	100	100	100	100	100	100	100														2	2	1	0	
60	97	98	99	92	99	99	99	99	99	98	98	98	98	T4	T6												3	3	2	1	0
61	97	98	100	100	98	97	98	99	98	99	100	100	99	T8	T10												3	3	2	1	0
62	100	100	100	100	100	100	100	100	100	100	100	100	100	T5	T6												3	3	3	2	2
63	96	97	97	96	95	95	96	97	96	97	97	96	96	T8	T9	T10											3	3	3	2	1
64	100	98	97	98	98	97	97	97	98	98	98	98	99	T4	T6												3	3	2	2	1

S. no.	MBS_150	MBS_180	MBS_210	MBS_240	MBS_270	MBS_300	MBS_330	MBS_360	VAS_0	VAS_30	VAS_60	VAS_90	VAS_120	VAS_150	VAS_180	VAS_210	VAS_240	VAS_270	VAS_300	VAS_330	VAS_360	First rescue analgesic	Time to onset of sensory block (in minutes)	Time to maximum sensory level (in minutes)
1									0	0	0	0	0	1	1	3	5	3	2	2	2	Tramadol	8	15
2									0	0	0	5										Tramadol	6	8
3									0	0	0	0	0	1	2	3	5	3	2	4	2	Tramadol	2	6
4									0	0	0	0	1	2	2	4	2	2	4	2	2	Tramadol	4	15
5									0	0	0	0	4	2	1	1	0	0	0	0	0	Tramadol	2	8
6									0	1	2	4	3	1	1	4	3	2	1	1	1	Tramadol	6	15
7									0	0	0	5	3	2	1	1	4	2	2	1	1	Tramadol	6	10
8																								
9									0	1	2	3	6	3	5	3	2	2	2	2	2	Tramadol	4	15
10																								
11									1	3	3	6	3	3	3	4	2	2	2	2	2	Tramadol	4	10
12									0	0	0	0	1	3	5	3	2	2	4	2	2	Tramadol	10	15
13	1	0							0	0	0	0	0	0	0	1	4	2	4	3	2	Tramadol	2	10
14									0	0	0	1	1	1	3	5	4	3	2	2	2	Tramadol	6	10
15									2	4	3	2	1	1	4	3	2	2	1	1	1	Tramadol	6	15
16									0	0	0	0	0	1	2	3	4	3	3	2	2	Tramadol	8	15
17	2	1	0						0	0	0	0	0	0	0	0	1	3	5	3	2	Tramadol	4	4
18									0	0	0	1	1	2	3	3	4	2	0	0	0	Tramadol	2	8
19									0	0	0	0	1	2	4	3	5	3	2	3	3	Tramadol	15	15
20	0								0	0	0	0	0	0	0	1	2	4	2	2	2	Tramadol	6	15
21									0	0	0	0	2	2	3	5	4	3	4	3	2	Tramadol	8	30
22									0	0	0	0	0	0	2	4	2	2	4	2	2	Tramadol	8	8
23									0	0	0	0	0	2	4	2	2	4	2	0	0	Tramadol	6	15
24	0								0	0	0	0	0	2	2	4	1	1	0	1	1	Tramadol	4	30
25									0	0	2	2	4	3	5	3	4	3	2	3	3	Tramadol	6	10
26									0	2	5	3	4	3	4	2	3	2	2	1	1	Tramadol	4	30
27									0	0	0	0	2	4	3	2	2	2	4	2	2	Tramadol	8	8
28	0	0							0	0	0	0	0	0	0	0	2	4	2	1	1	Tramadol	6	10
29									0	2	4	2	2	4	3	2	3	2	3	2	2	Tramadol	10	10
30									0	0	2	2	4	2	3	4	2	2	3	3	3	Tramadol	15	30
31									0	2	4	2	3	3	4	3	2	2	2	2	2	Tramadol	15	30
32												3	4	3	4	3	3	3	3	3	4	Tramadol	4	30
33									0	2	4	2	2	3	4	2	2	2	1	2	2	Tramadol	8	30
34									1	3	5	1	1	2	3	3	6	3	3	2	2	Tramadol	4	30
35									0	0	0	1	2	2	2	3	4	3	2	2	2	Tramadol	4	10
36									0	0	0	0	0	2	4	2	2	1	1	1	1	Tramadol	4	15
37																								
38									0	0	0	0	0	1	2	3	4	3	2	2	2	Tramadol	4	10
39									2	3	2	3	3	3	3	3	4	2	2	2	2	Tramadol	10	10
40									0	0	0	0	2	3	4	3	2	2	2	2	2	Tramadol	15	15
41									0	0	0	2	4	2	2	2	2	3	4	2	2	Tramadol	15	15
42	1	0							0	0	0	0	0	0	0	0	1	2	4	2	1	Tramadol	10	15
43									0	0	0	0	0	0	1	3	4	1	1	1	1	Tramadol	6	10
44									0	0	1	3	4	2	2	2	4	1	1	1	1	Tramadol	30	45
45									0	0	0	0	0	1	3	4	2	2	2	4	2	Tramadol	4	15
46									0	0	0	1	2	4	2	1	3	4	2	1	1	Tramadol	6	30
47	1	0							0	0	0	0	0	0	0	1	1	3	4	1	2	Tramadol	6	30
48	1	0							0	0	0	0	0	0	1	2	4	3	2	2	4	Tramadol	4	15
49									0	0	0	0	2	2	4	2	0	1	2	3	3	Tramadol	4	15
50	0	0							0	0	0	0	0	0	2	4	3	2	4	1	1	Tramadol	10	10
51									0	0	0	0	2	4	1	1	2	4	1	2	2	Tramadol	4	15
52	1	0							0	0	0	0	0	0	0	0	1	2	4	2	2	Tramadol	4	10
53																								
54									0	0	0	0	1	2	4	2	1	1	2	1	1	Tramadol	6	15
55	0								0	0	0	0	0	0	0	1	3	4	1	1	1	Tramadol	4	10
56	1	0							0	0	0	0	0	0	0	1	2	5	2	1	1	Tramadol	6	10
57									0	0	0	0	2	4	2	2	4	2	1	2	2	Tramadol	4	10
58	0								0	0	0	0	0	1	3	4	2	2	4	3	2	Tramadol	4	4
59									0	0	0	0	2	4	2	2	1	4	2	2	1	Tramadol	4	15
60									0	0	0	0	0	0	0	2	4	2	1	1	1	Tramadol	2	4
61									0	0	0	0	0	4	2	4	2	2	3	4	2	Tramadol	4	8
62	1	0							0	0	0	0	0	0	1	2	4	2	2	4	2	Tramadol	4	15
63	0								0	0	0	0	0	0	0	2	4	1	3	4	2	Tramadol	8	10
64	0								0	0	0	0	1	2	4	2	2	4	2	2	2	Tramadol	6	30

S. no.	Duration of sensory block (in minutes)	Time to onset of motor block (in minutes)	Total duration of motor block (in minutes)	Duration of analgesia (in minutes)	Time of occurrence of Side effect	Treatment administered	Time of occurrence of Side effect	Treatment administered	Time of occurrence of Side effect	Treatment administered	Time of occurrence of Side effect	Treatment administered	Time of occurrence of Side effect
1	110	6	170	300					as charted	I/V Ephedrine 6mg Bolus			4:30 PM
2	90	2	240	270									
3	90	4	100	310									
4	105	2	185	315									
5	80	4	140	210									12:35 PM
6	90	4	185	185									12:25 PM
7	90	15	90	145									
8													
9	105	8	120	255									
10													
11	90	4	180	272							12:00 PM	Atropine 0.6 mg	
12	90	10	185	275									
13	90	4	210	300									
14	90	6	130	310									3:10 PM
15	105	4	150	185									
16	90	15	160	280									
17	60	4	305	395									
18	85	2	190	310	2:35 PM	Inj. Ondansetron 4 mg							
19	120	15	195	300									4:45 PM
20	105	4	240	360									
21	90	10	165	375									
22	90	15	90	275									
23	105	4	210	300									
24	100	6	235	295									
25	45	6	150	180									
26	105	6	180	240									
27	75	4	175	235									
28	110	4	200	320									
29	90	4	210	210									
30	60	30	75	170									
31	105	4	210	210									
32	120	2	230	230					2:30 PM	Ephedrine bolus			
33	90	8	120	180									
34	120	4	180	240									
35	75	4	135	315									
36	90	6	165	255									
37													
38	90	4	215	335					At mentioned time points	Ephedrine Boluses			
39	75	4	200	320									
40	90	15	125	245									
41	75	10	155	245									
42	45	10	235	360									
43	90	4	195	345									
44	90	8	165	255									
45	90	2	210	300									
46	90	4	160	280									
47	60	4	262	382									
48	135	4	255	315									2:30 PM
49	90	4	174	270									
50	113	4	218	278									
51	90	2	235	295									6:50 PM
52	75	2	290	420									
53													
54	90	6	125	275									
55	90	4	185	305									
56	90	4	270	360									
57	90	4	210	270									
58	90	2	270	330									4:00 PM
59	90	2	255	315									1:45 PM
60	90	4	180	300									
61	120	4	210	240									
62	120	2	285	345									1:45 PM
63	105	6	215	305					10:00 PM	Inj. Ephedrine 6 mg			
64	105	4	225	255									

S. no.	Treatment administered	Time of occurrence of Side effect	Treatment administered	Time of occurrence of Side effect	Treatment administered	Remarks
1	warming with blanket					
2						
3						
4						
5	warming done					
6	warming done					
7						
8						Converted to GA
9						
10						Converted to GA
11						
12						
13						
14	warming done					
15						
16						
17						
18						
19	Tramadol 50mg+ warming done					
20		3:15 PM	Calamine Lotion			
21						
22						
23						
24						
25						
26						
27						
28						
29						
30						
31		At 7 mins	Inj. Hydrocort 100 mg			
32						
33						
34						
35						
36						
37						Converted to GA
38						
39						
40						
41						
42						
43						
44						
45						
46						
47						
48	Warming with blankets					
49						
50						
51	Warming with blankets					
52						
53						Converted To GA
54						
55						
56						
57						
58	Warming with blankets					
59	Warming with blankets					
60						
61						
62	Warming with blankets					
63						
64						

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No. BFUHS/2K23p-TH/ 13150 Date 27/12/23

The Principal
Dayanand Medical College & Hospital
Ludhiana

Subject:: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Purnima Bhanot**, a student of your college for **MD Anaesthesiology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Comparative study of hyperbaric ropivacaine 0.75% and hyperbaric bupivacaine 0.5% for spinal anaesthesia .

Supervisor
Dr. Richa Jain
Assoc. Professor
Dept. of Anaesthesiology,

Co-Supervisor:-
Dr. Shikha Gupta
Professor
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1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% AND HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

ANAESTHESIOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

AUGUST, 2022

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ABSTRACT OF PLAN OF THESIS

Title	COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% AND HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA
For the degree of	MD Anaesthesia
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University	Baba Farid University of Health Sciences, Faridkot

Introduction: Though bupivacaine is the most commonly used intrathecal local anaesthetic because of its long duration of sensory and motor blockade, the reports of CNS and CVS toxicity associated with it led to research of a better alternative for spinal anaesthesia. Studies have reported that hyperbaric 0.5% ropivacaine produce reliable subarachnoid block but of shorter duration than hyperbaric 0.5% bupivacaine. Hence, we plan to evaluate the anaesthetic efficacy and safety of equipotent doses of 0.75% hyperbaric ropivacaine compared to 0.5% hyperbaric bupivacaine in combination with fentanyl for spinal anaesthesia in lower limb surgeries.

Aim of Study: To compare the efficacy and safety in terms of onset and duration of sensory and motor block, of 0.75% hyperbaric ropivacaine with 0.5% hyperbaric bupivacaine in spinal anaesthesia.

Materials & methods: A prospective randomized double blind study is planned to be conducted on 60 adult ASA grade I, II, III patients posted for lower limb surgeries under spinal anaesthesia after taking a written informed consent. Enrolled patients will be randomly divided into two equal groups to receive either 2.5ml of 0.75% hyperbaric ropivacaine with 25µg fentanyl or 2.5ml of 0.5% hyperbaric bupivacaine with 25µg fentanyl in subarachnoid block. Patient will be observed for duration of sensory block, time of onset of sensory block, maximum sensory level, time to achieve maximum sensory level, time to complete motor block, time, total duration of motor block, duration of analgesia and hemodynamic parameters. The data thus collected will be statistically analyzed.

Clinical Significance: This study will help us to evaluate hyperbaric 0.75% ropivacaine in terms of clinical efficacy and safety profile in comparison to hyperbaric 0.5% bupivacaine for use in lower limb surgeries under spinal anaesthesia.

Keywords: Ropivacaine, bupivacaine, fentanyl, lower limb surgeries, spinal anaesthesia, local anaesthetic.

(Signature) Candidate	(Signature) Co-supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% AND HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA"** exist in the Department of Anaesthesia at Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

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APPROVAL PROFORMA
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5.	TITLE OF THE TOPIC	COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% AND HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA.

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Subarachnoid block [SAB] has gained popularity among anaesthesiologists for lower limb surgeries because of the ease of administration, maintenance of consciousness and spontaneous respiration, adequate muscle relaxation along with benefit of prolonged post operative analgesia. It is a preferred technique over general anaesthesia due to its benefits of lower operative costs, reduced incidence of major perioperative complications like deep vein thrombosis, pulmonary embolism, respiratory complications, decreased stress response to surgery, decreased intraoperative blood loss and substantial pain in early post operative period.[1] Thus SAB has always remained the preferred mode of anesthesia for lower limb surgeries. However, SAB is associated with adverse effects such as - hypotension, bradycardia, inadequate or failed block, postdural puncture headache, backache, urinary retention, meningitis etc. [2]

Various local anaesthetic agents have been employed for spinal anaesthesia. Bupivacaine is the most commonly used intrathecal local anesthetic because of its long duration of action and significant duration of sensory and motor blockade[3]. It is a long acting local anesthetic [1-butyl-2',6' pipecolxylidine] which was first synthesized in 1957 by Ekenstan in Sweden, after which it underwent various trials and eventually achieved acceptance in virtually every area of local anaesthesia [LA] practice.[4]

Ropivacaine, another long acting amide local anaesthetic, is almost similar to bupivacaine in chemical structure. Due to less lipid solubility and stereoselective structure, ropivacaine has significantly higher threshold for cardiotoxicity and CNS toxicity than bupivacaine. Thus it was introduced in clinical practice with the claim to be less cardiotoxic than bupivacaine.[5] Initially it was available in isobaric forms with different concentrations which soon made its place into the arena of regional anaesthesia.

However, due to unpredictable spread of isobaric ropivacaine its use as an intrathecal anaesthetic agent became limited.

Based on the findings that hyperbaric solutions of ropivacaine produced a more consistent block than the plain one, studies compared 0.5% hyperbaric ropivacaine (made by adding glucose) with 0.5% hyperbaric bupivacaine and revealed that ropivacaine provides shorter duration of sensory and motor block as well as it is less potent than bupivacaine.[6] In a trial involving lower limb surgeries the duration of sensory block with ropivacaine 15mg was found to be similar with bupivacaine 10 mg and the motor block was significantly shorter.[7] It was also suggested that on a milligram for milligram basis, the potency of ropivacaine relative to bupivacaine is two- thirds with regard to sensory block and half with regard to motor block.[8]

Since hyperbaric preparations of ropivacaine 0.75% were unavailable, few studies compared reconstituted hyperbaric 0.75% ropivacaine (prepared by adding glucose to isobaric ropivacaine) with hyperbaric 0.5% bupivacaine for clinical efficacy under spinal anaesthesia in lower limb surgeries and revealed that hyperbaric 0.75% ropivacaine is a better alternative to hyperbaric 0.5% bupivacaine with better block characteristics and hemodynamic stability.[9] Recently, hyperbaric preparation of 0.75% ropivacaine equipotent to 0.5% hyperbaric bupivacaine has been commercially launched after conducting a successful phase 3 multicentric trial where 0.75% hyperbaric ropivacaine has shown comparable efficacy and better safety profile in comparison with 0.5% hyperbaric bupivacaine when used by intrathecal route.

Addition of intrathecal opioids have become a favorable and preferred adjuvant to LA in spinal anesthesia. They intensify the sensory block without increasing the sympathetic blockade and also diminish the side effects associated with high dose of LA.[10] It has also been associated with decreased pain scores and reduced analgesic requirements in the post operative period making it popular for lower limb surgeries.

Since, there is limited study on efficacy of hyperbaric ropivacaine 0.75% with fentanyl in spinal anaesthesia; we propose a prospective randomized study to compare equipotent doses of hyperbaric 0.75% ropivacaine and 0.5% hyperbaric bupivacaine in combination with fentanyl for spinal anaesthesia in lower limb surgeries.

6.2 REVIEW OF LITERATURE

Karl August Bier introduced spinal anesthesia in 1898. Spinal anaesthesia also called subarachnoid block or intrathecal block is a type of regional anesthesia where the local anaesthetic is injected into the subarachnoid space through a very fine 23G/ 26G needle (preferably dura splitting needle since it has a lesser incidence of post dural puncture headache). This results in blockade of sensory and motor fibers along with sympathetic blockade. Regional anaesthesia has advantage over general anaesthesia that it is less toxic. Thus after the discovery of SA, various drugs were studied to be used as local anaesthetics which were given intrathecally to improve the quality of block. [11]

The journey of Intrathecal local anaesthetics started with James Leonard Corning, who described the use of cocaine for spinal anesthesia.[12] After that, a number of studies were done on various local anesthetic drugs on the lines of safety and efficacy which resulted in evolution of LA from cocaine to lidocaine to bupivacaine which is most commonly used these days.

Bupivacaine is an amide local anesthetic with a piperidine ring structure due to which bupivacaine and the other congener drugs like mepivacaine, ropivacaine etc are known as Pipecholyl xylidines. Bupivacaine has rapid onset of action usually within 5 minutes, is of long duration with profound conduction blockade.[3] It was observed that the use of hyperbaric local anaesthetic solutions in comparison to isobaric solutions,results not only in a more predictable cephalad spread, but also increases the duration of the clinically useful block (given by duration at the T10 dermatome) with a more rapid regression of sensory block and recovery from motor block[13]

After the introduction of bupivacaine in the market its increased usage in spinal anaesthesia paralleled the progressive and cumulative reports of CNS and CVS toxicity. Numerous experimental studies were conducted to identify the fine cellular mechanism of this toxicity and for better understanding of the action of local anesthetics. This led to identification of

optically active isomers of the mepivacaine family and selection of ropivacaine to be used intrathecally to produce subarachnoid block. Ropivacaine is a pure S(-) enantiomer. It is almost similar in structure to bupivacaine except for the functional group on the piperidine nitrogen atom which is propyl group in case of ropivacaine while butyl group in case of bupivacaine. Ropivacaine is structurally shorter in length due to the less number of carbon atoms as compared to bupivacaine which makes the former less lipid soluble. Its toxicology was selectively and extensively studied before its introduction into the market in 1996.[14]

Effect of LA is directly related to the myelination and size of the nerve fibers. The more lipophilic local anaesthestics penetrate large myelinated motor fibers more effectively than the less lipophilic local anaesthetics. Being less lipophilic, ropivacaine penetrates less into large myelinated motor fibers like Aβ which are involved in motor function. It has selective action on the pain transmitting Aδ and C fibres. It has been found that in equipotent doses the degree of motor blockade is less pronounced with ropivacaine. Thus ropivacaine shows more selective sensory blockade than bupivacaine which is lipophilic and produce profound sensory and motor block.[15]

Ropivacaine has been used for epidural anaesthesia in caesarean section and hip or lower limb surgeries; for spinal anaesthesia in place of bupivacaine for sensory and motor blockade and in peripheral nerve blocks for both surgical anaesthesia and postoperative pain management.[16] Isobaric solutions of ropivacaine were studied for many years but it was concluded that a higher dose of isobaric ropivacaine needs to be given intrathecally to produce same sensory and motor blockade as bupivacaine without producing any significant advantage.[17]

Eventually hyperbaric solutions of ropivacaine were made and used to study the effect of hyperbaric 0.5% ropivacaine in comparison to hyperbaric 0.5% bupivacaine in lower limb and hip surgeries. Dar FA et al published a study where hyperbaric solution of 0.5% ropivacaine was

prepared aseptically by mixing 5 ml of 0.75% isobaric ropivacaine with 2 ml of 25% dextrose and 0.5 ml sterile water at room temperature. This gave a total volume of 7.5 ml resulting in a final glucose concentration of 6.6% in hyperbaric ropivacaine solution. The prospective study was done among 200 patients aged 40-75 years randomly divided into 2 groups. The mean onset of sensory block at T-10 level (6 ± 1.3 min vs. 3 ± 1.1 min; P < 0.001) and motor block (13 ± 1.6 min vs. 9 ± 1.3 min; P < 0.001) was significantly slower in ropivacaine group as compared to bupivacaine group. The mean duration of sensory block was significantly shorter with ropivacaine group (160 ± 12.9 min) than with bupivacaine group (260 ± 16.1 min; P < 0.001). The mean duration of motor block was also shorter in the ropivacaine group compared to bupivacaine group (126 ± 9.2 min vs. 174 ± 12.6 min; P<0.001). The intraoperative quality of anaesthesia was similar in both groups (P=0.4). Thus it was concluded in the study that hyperbaric bupivacaine used intrathecally has a faster onset of sensory block and prolonged duration of analgesia compared to hyperbaric ropivacaine.[18]

Ghimire R et al conducted a prospective, randomized, double blind study, to compare the effectiveness and safety between 0.5% hyperbaric bupivacaine and 0.5% hyperbaric ropivacaine among 60 patients using 3 ml of 0.5% hyperbaric bupivacaine with glucose 8% and 3ml of 0.5% hyperbaric ropivacaine with glucose 8.33%. It was concluded that the time to onset of maximum sensory block level was faster in bupivacaine (9.10±3.90min) than in ropivacaine (10.87±5.37min) and statistically not significant. The time to 5 segments regression was faster in ropivacaine (116.00±29.72min) than bupivacaine (143.50±18.76min) and the time to S2 level regression of sensory block was faster in ropivacaine (154.00±27.84min) than bupivacaine (186.00±18.73min). The time to onset of the maximum motor block was faster with bupivacaine (8.70±3.19min) as compared to ropivacaine (13.10±4.40min).Their final impression was that hyperbaric ropivacaine (3ml, 0.5%) provides a reliable

subarachnoid block of shorter duration than hyperbaric bupivacaine (3ml, 0.5%) with stable hemodynamic parameters.[19]

Chatterjee S et al reconstituted 0.75% hyperbaric ropivacaine with glucose 50% and compared its efficacy with 0.5% hyperbaric bupivacainein 100 ASA I and II patients posted for lower limb surgeries under spinal anaesthesia. He found that patients who received ropivacaine experienced significantly late onset and shorter duration of sensory and motor block in comparison to patients who received bupivacaine. There were clinically insignificant differences in perioperative hemodynamics and side-effects noted in each group. It was observed in this study that equipotent dose of hyperbaric ropivacaine had shorter duration of analgesia and anesthesia than hyperbaric bupivacaine.[20]

To further intensify the level of sensory block and for better analgesia, intrathecal opioids were introduced as adjuvants to spinal drugs. Intrathecal opioids are synergistic to LA as they produce similar effect by acting on different receptors. LA bind at nerve axon level while intrathecal opioids bind to opioids receptors located in laminae I and II at the spinal dorsal horn reducing nociceptive transmission.[21] They intensify the sensory block without increasing the sympathetic blockade and also diminish the side effects associated with high dose of LA. They also help in prolonging the duration of postoperative analgesia and offer hemodynamic stability.[10] Amongst all opioids fentanyl is the most commonly used. Compared with I/V fentanyl, Intrathecal fentanyl decreased visceral and somatic pain and improved the quality of block. It has also been associated with decreased pain scores and reduced analgesic requirements in the post operative period making it popular for lower limb surgeries. The near absence of respiratory depression with fentanyl (with permissible dose of 25 µgm) ,better pulmonary spirometric function and shorter hospitalization makes it an ideal drug for intrathecal use.[22]

Various studies have observed that intrathecal opioids have a synergistic effect when used with local anaesthetics in spinal anesthesia. Chaudhary A et al conducted a study on 60 male patients of ASA I- III posted for TURP, where Group A (n=30) received intrathecal injection of ropivacaine 2 ml (0.75%) and Group B (n = 30) ropivacaine 1.8 ml (0.75%) with fentanyl 10 µg (0.2ml). The characteristics of onset and regression of sensory and motor blockade, hemodynamic stability, and side effects were observed. The highest level of sensory block was at T10 in group A and T9 in group B (P = 0.001). Duration of motor block was longer in group B being 210.51 ± 61.25 min than in group A being 286.25 ± 55.65 min (P < 0.001). They concluded that addition of fentanyl to ropivacaine may offer the advantage of shorter duration of motor block and hemodynamic stability without any increase in the frequency of major side effects.[23]

To find out the clinical efficacy of intrathecal opioids when used along with hyperbaric solution of 0.75% ropivacaine, A Khunongbham K et al performed a comparative double blinded randomized study on 60 ASA I and II patients posted for lower abdominal and lower limb surgeries. He reconstituted hyperbaric 0.75% ropivacaine and hyperbaric 0.5% bupivacaine solutions. 30 patients received hyperbaric 0.5% bupivacaine (2 ml) with fentanyl 0.4 ml and normal saline (0.25 ml) while other 30 patients received ropivacaine 0.75% (2 ml) with fentanyl 0.4 ml, 0.2 ml of 50% dextrose and normal saline (0.05 ml). The spinal block characteristics and hemodynamic parameters were recorded and statistically analyzed. There was no difference between the two groups in the mean time to attain highest sensory block level (group R 9.10 ± 1.97 min; group B 9.17 ± 1.51min; P > 0.05) and median maximum extent (ropivacaine T6; bupivacaine T5; P > 0.05); but the mean duration of sensory block regression to S2 was significant (ropivacaine 157.44 ± 17.78 min; bupivacaine 180.60 ± 23.06 min; P < 0.001). The degree of motor block by 5 min was significantly different between the groups (ropivacaine 1.50 ± 0.82; bupivacaine 2.40 ± 0.49; P < 0.001). Patients receiving ropivacaine

mobilized sooner (ropivacaine 115.47 ± 17.07 min; bupivacaine 154.60 ± 20.37 min; $P < 0.001$) . Thus it was concluded that ropivacaine 15 mg with fentanyl 20 µg was a better alternative to bupivacaine (heavy) 10 mg with better block characteristics and hemodynamic stability.[9]

Taken together, these studies suggest that hyperbaric 0.75% ropivacaine can be used as an alternative to hyperbaric 0.5% bupivacaine for spinal anaesthesia. The use of hyperbaric ropivacaine 0.75% as intrathecal local anaesthetic agent for spinal anaesthesia may aid in early ambulation of patient with lesser haemodynamic instability and thus its blocking characteristics needs to be evaluated for spinal anaesthesia.

6.3 AIMS AND OBJECTIVES OF THE STUDY

To compare the efficacy and safety, in terms of onset and duration of sensory and motor block, of hyperbaric 0.75% ropivacaine versus hyperbaric 0.5% bupivacaine in combination with fentanyl in spinal anaesthesia for lower limb surgeries.

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7. MATERIAL AND METHODS

7.1 SOURCE OF DATA

A prospective, randomized, double-blind study is planned to be conducted in Department of Anaesthesiology after approval from the Institutional Ethics Committee on 60 adult patients posted for lower limb surgeries under spinal anaesthesia. A written informed consent will be obtained from all the patients included in the study.

7.2 METHOD OF COLLECTION OF DATA

Inclusion Criteria-

1. Patients aged between 18-65 years of either gender scheduled for lower limb surgery under spinal anaesthesia.
2. American Society of Anaesthesiologists (ASA) grade I, II and III.

Exclusion Criteria-

1. Patient refusal for subarachnoid block.
2. Allergy to local anaesthetic drugs or any history of anaphylactic reaction to the drugs used.
3. Frank coagulopathy evidenced by history and laboratory investigations.
4. Infection at injection site.
5. Patients with spinal deformities like kyphoscoliosis and scoliosis etc.
6. Patients with history of pre-existing neurological disease.
7. Unable to comprehend sensory and motor block.

GROUP ALLOCATION

Patients will be randomly allocated to either of the two groups- Group R and B of 30 patients each by computer generated random numbers contained in sealed, sequentially numbered envelopes. The study will be made double blind as the patient and the investigator will be unaware of the nature of drug used. The name of the drug used will be sealed in an envelope which will be opened by the anaesthetist administering spinal anaesthesia.

Group R - Patients will receive 3ml of intrathecal drug which will include 2.5ml of 0.75% hyperbaric ropivacaine and 25µg (0.5 ml) fentanyl.

Group B- Patients will receive 3ml of intrathecal drug which will include 2.5ml of 0.5% hyperbaric bupivacaine and 25µg (0.5 ml) fentanyl.

METHODOLOGY

PREANAESTHETIC CHECK UP

Each patient included in this study will undergo a preanaesthetic evaluation (PAC) one day prior to the planned surgery in which thorough history taking, general physical and systemic examination will be done. PAC will include any known drug allergies, prior surgical and anaesthetic exposure, detailed systemic evaluation to rule out any cardiac, neurological, endocrine, hepatic or respiratory disorders. It will also be used as a tool to document patient's baseline vital parameters and all the necessary routine investigations which will include hemogram, renal function tests, coagulation profile and chest X-ray. During the evaluation of the patients, they will be explained about visual analogue scale (VAS) which will be used to measure the post operative pain.

PREMEDICATION

All patients will be instructed to follow the nil per oral guidelines and maintain ≥8 hours of fasting for solids and ≥2 hours of fasting for clear fluids. Night before the surgery all patients will receive tablet alprazolam 0.25mg followed by tablet pantoprazole 40mg on the morning of surgery with sips of water. On arrival in preoperative area, I.V. access will be established using 18G cannula.

ANAESTHESIA TECHNIQUE

On arrival in the operating room (OR), the patients will be positioned on the operating table in the supine position and monitored with continuous electrocardiography (ECG), cyclic noninvasive blood pressure (NIBP), and peripheral oxygen saturation (SpO2). Mean of three consecutive readings of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and SpO2

at one minute interval will be recorded as baseline. All patients will be administered 10 mL/kg of crystalloids intravenously before the onset of spinal anaesthesia.

The drug code to be given will be sealed in an envelope and 60 such envelopes will be made for all the cases. The envelope will be opened by the designated anaesthesiologist who will load the mentioned drug in a 5cc syringe along with adjuvant (fentanyl). The drug thus loaded will be handed. Over to the attending anaesthesiologist in a coded form who will be blind to the nature of drug used. Under all aseptic precautions and with patients placed in sitting position, skin infiltration of L3-L4 interspace with 2ml of 2% lignocaine will be performed followed by lumbar puncture at same interspace with a 26G Quincke needle using a midline approach. Group R (25 patients) will receive 3ml of intrathecal drug which will include 2.5ml of 0.75% hyperbaric ropivacaine and 25µg fentanyl and Group B (25 patients) will receive 3ml of intrathecal drug which will include 2.5ml of 0.5% hyperbaric bupivacaine and 25µg fentanyl. The bevel of the needle will be kept cranial during injection. After free flow of cerebrospinal fluid is verified, anaesthetic solution will be injected at rate of 0.2ml/sec. Patients will be immediately placed in a supine position after the spinal anesthesia with OR table in neutral position. The drug used will be decoded after the completion of study.

INTRAOPERATIVE ASSESSMENT

Immediately after the intrathecal injection (taken as 0 min) HR, SBP, DBP**,** MBP and SpO2 will be recorded. Patients will be assessed for the level of sensory block using a pinprick method with a sterile 26G needle pricked in mid clavicular line on either side. Level of sensory blockade will be noted at 0 min, 2min, 4min, 6min, 8 min, 10 min, 15 min and thereafter every 15 minutes till two dermatome regression from maximum level of sensory block. The surgery will be allowed to commence after sensory block has reached T10. The degree of motor block in the lower limbs will be assessed using a Modified Bromage Scale (MBS)[9] at 0 min, 2min, 4min,

6min, 8 min, 10 min, 15 min and thereafter every 15 minutes till onset of motor block.

Modified Bromage Scale[9] –

0= free movement of legs and feet

1= unable to raise the extended legs but able to flex knees with free movement of feet

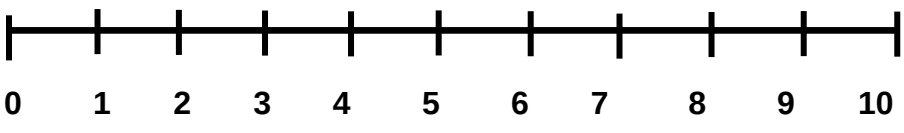
2= unable to flex knees but with the free movement of feet

3= unable to move legs and feet.

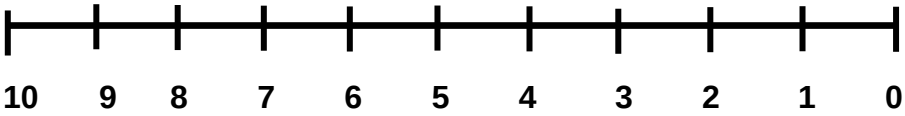
Hemodynamic parameters will be assessed at 0 min, 2min, 4min, 6min, 8 min, 10 min, 15 min and thereafter every 15 minutes throughout the surgery. Hypotension, defined as a fall in systolic blood pressure >20% from the baseline will be treated with IV injection of ephedrine 6 mg and IV fluids. A fall in heart rate <50 beats/min will be considered as bradycardia and treated with injection atropine 0.6 mg IV. After completion of the surgery the hemodynamic parameters as well as the level of sensory and motor block will be documented and then the patient will be shifted to Post Anaesthesia Care Unit (PACU).

POSTOPERATIVE ASSESSMENT

Upon shifting the patient in post anesthesia care unit, the HR, MAP, SBP, DBP, SpO_2, VAS and MBS of the patient will be recorded. The MBS will be recorded every 30 minutes till complete recovery of motor block. Haemodynamic parameters will be assessed hourly. Pain will be assessed using visual analogue scale (VAS)- it's a 10 point scale wherein 0 indicates no pain and 10 indicates worst imaginable pain. It will be assessed hourly for 6 hours post-operatively.



No pain **Worst pain**



Worst pain **No Pain**

Time to first analgesic demand will be noted when VAS will be more than 4 and patient will be given Inj. Tramadol 100mg IV. Hospital protocols will be followed for pain management. Any side effects (discomfort, nausea, vomiting, shivering, pruritis, hypotension and bradycardia) in six hours postoperatively will be recorded and any intervention required will be noted. All the parameters will be noted by the assessor who will be blinded to the local anaesthetic drug used. Patients with failed spinal anaesthesia and subsequent conversion to general anaesthesia will be excluded from the study.

OUTCOMES OF THE STUDY

PRIMARY OUTCOME

Duration of sensory block (minutes)- The duration of sensory block will be defined as the period from intrathecal injection till two dermatome regression from maximum level of sensory block (in minutes).

SECONDARY OUTCOMES

1. The onset of sensory block (minutes) - The onset of sensory block will be defined as the time between injection of intrathecal anaesthetic and the absence of pain at T10 dermatome assessed by pinprick test.
2. Maximum level of sensory block
3. Time required to achieve maximum level of sensory block (minutes)
4. Time required for onset of motor block (minutes) - Time for onset of motor block will be defined as the period from intrathecal injection till the MBS is grade 3.

5. Total duration of motor block (minutes) – It is defined as the period from intrathecal injection till complete motor block recovery (MBS-grade 0).
6. Duration of analgesia – It will be defined as period from onset of sensory block to the time for first rescue analgesic demand or when the VAS is ≥4.
7. Episodes of hypotension and bradycardia

SAMPLE SIZE CALCULATION

The formula used is as under:

$n = (\sigma 12 + \sigma 22) (Z\alpha + Z\beta)^2/(m1 – m2)^2$

Where,

Zα = Value of standard normal variate corresponding to α level of significance (1.96)

Zβ = The standard normal deviate for desired power (0.842)

m = Average

σ = Standard deviation

Assumptions:

From the Pilot study

Mean Group (m1) = 67.5

Mean Group (m2) = 56.25

Coefficient of variation = 150%

Standard deviation Group (σ1) = 15

Standard deviation (σ2) = 14.36

With the above assumptions the sample size for 95% confidence level & 80% power works out 27 in each group. So we will take 30 each cases.

STATISTICAL ANALYSIS

Results will be expressed as mean values ± standard deviation (SD) or median value if appropriate. Categorical data will be compared using chi-square analysis, and for continuous data, t-test analysis will be used. All data will be analyzed by using Statistical Package of Social Sciences (SPSS Software Version 21). Results will be considered significant if $P < 0.05$.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ONPATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

8. LIST OF REFERENCES

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PROFORMA

S. No.	Patient Initials:
MRD No.	Randomization No:
Age/Sex:	Height:
Weight:	BMI:
ASA grade:	Comorbidities:
Diagnosis:	
Surgery Performed:	
Date of surgery:	
Time of administration of spinal anaesthesia:	
Time of start of surgery:	
Time of completion of surgery:	
Duration of Surgery:	
Time of patient received in PACU:	
Total duration of motor block:	
Time of rescue analgesic administration:	

PREOPERATIVE INVESTIGATIONS

Investigation	**Lab Values**
Hemoglobin	
Total leucocyte count	
Prothrombin Time/ International Normalized Ratio	

Signature of Candidate **Signature of Supervisor**

INTRAOPERATIVE OBSERVATIONS

Time in minutes	HR (beats/min)	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	SpO2 (%)	Sensory level	Modified Bromage Score	Vasopressor administered
Baseline (mean of 3 readings)								
0 (immediately after spinal injection)								
2								
4								
6								
8								
10								
15								
30								
45								
60								
75								
90								
105								
120								
150								
180								

NIBP Reading Before Administering Vasopressor			Amount Of Vasopressor Given	NIBP Reading After Administering Vasopressor		
SBP	DBP	MAP	DOSE	SBP	DBP	MAP

Maximum sensory level attained:

Amount of vasopressor needed to treat hypotension:

Total amount of I.V. fluids administered:

Signature of Candidate **Signature of Supervisor**

POSTOPERATIVE OBSERVATIONS

Time (min)	HR (beats/ min)	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	SpO2 (%)	Sensory level	Modified Bromage Score	VAS	Rescue Analgesic
0									
30									
60									
90									
120									
150									
180									
210									
240									
270									
300									
330									
360									

STUDY OUTCOMES

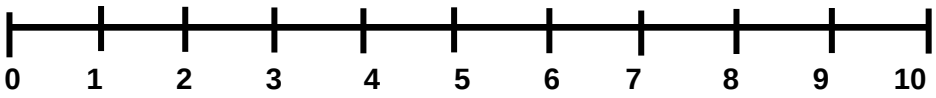
S.No.	Parameters	Duration (in minutes)
1.	Time to onset of sensory block	
2.	Time to maximum sensory level	
3.	Duration of sensory block	
4.	Time to onset of motor block	
5.	Total duration of motor block	
6.	Duration of analgesia	

Signature of Candidate **Signature of Supervisor**

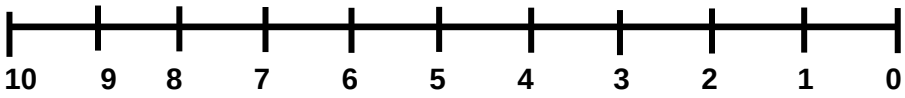
SIDE EFFECTS

Side Effects	Time of occurrence of Side effect	Treatment administered
Nausea/Vomiting		
Dizziness		
Hypotension		
Bradycardia		
Shivering		
Pruritis		
Others		

Visual Analogue Scale



No pain **Worst pain**



Worst pain **No Pain**

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I…….D/o, W/o, S/o……..…… am willing to participate in the study **"COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% AND HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

……. ……
Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "**COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____	_____
गवाह के हस्ताक्षर	रोगी के हस्ताक्षर/अंगूठे का निशान
नाम:	नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“COMPARATIVE STUDY OF HYPERBARIC ROPIVACAINE 0.75% AND HYPERBARIC BUPIVACAINE 0.5% FOR SPINAL ANAESTHESIA” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ